

FIG. 1A

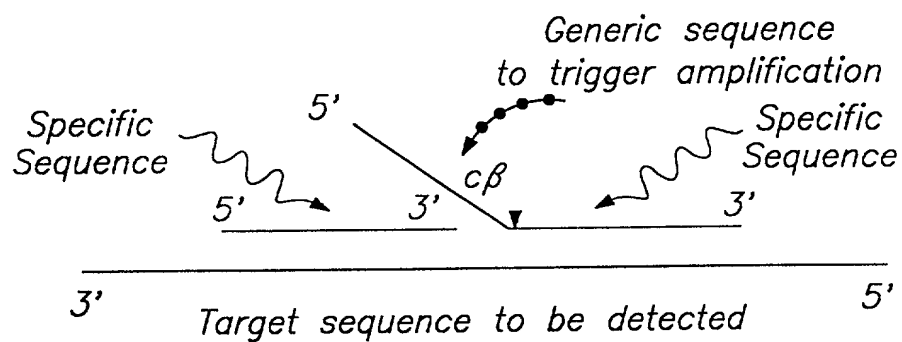


FIG. 1B PART ONE: TRIGGER REACTION

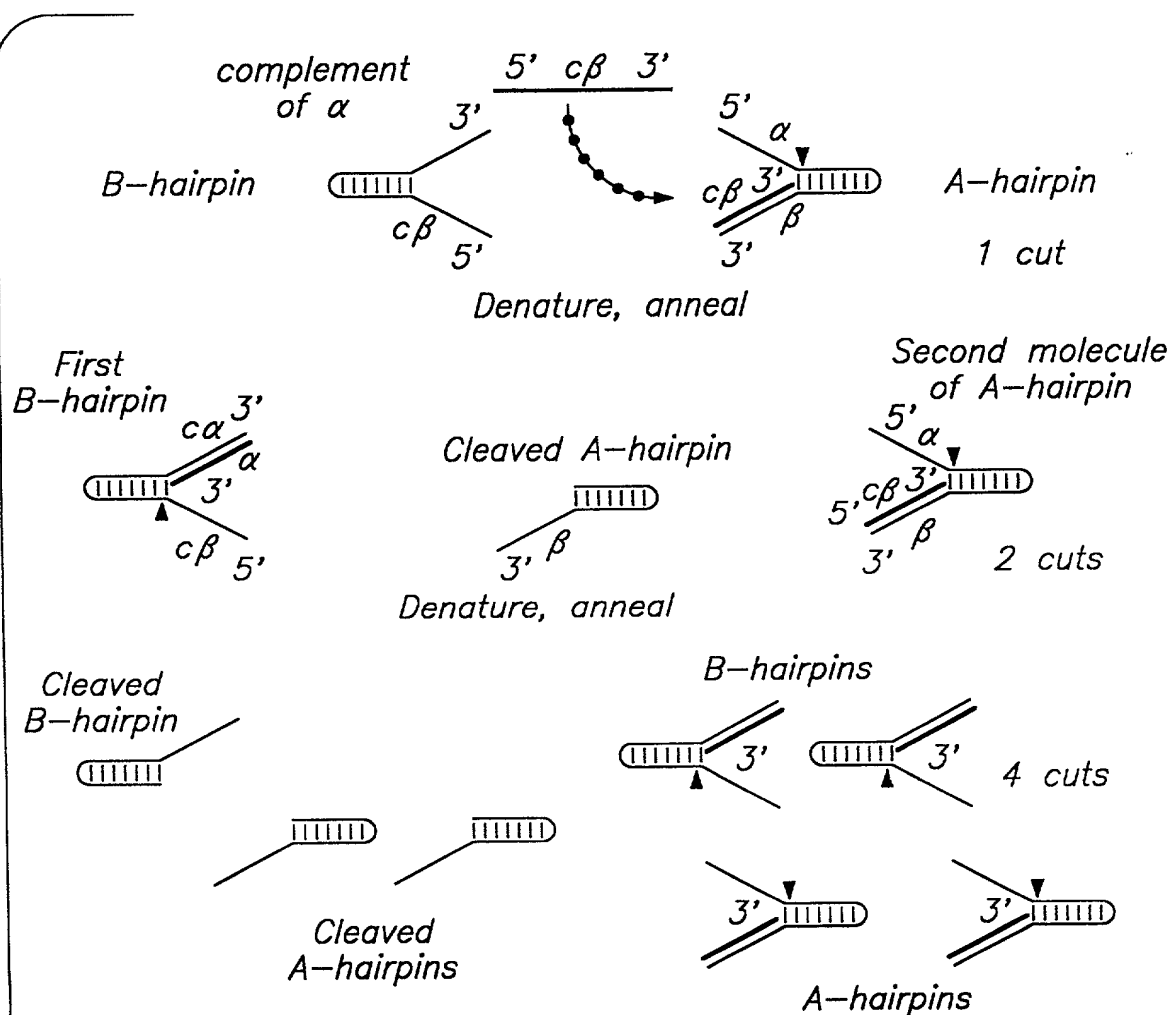


FIG. 1C PART TWO: DETECTION REACTION

| | | |
|----------|--|-----|
| MAJORITY | ATGXXGGCGATGCTTCCCCCTCTTTGAGCCCAAAAGGCCGGGTCTCCTGGTGACGGCACCCACCTGGCCT | |
| DNAPTAQ | ..AG..G.....G..... | 70 |
| DNAPTFL |C.G..... | 67 |
| DNAPTTH | ..GA.....G.....A..... | 70 |
| MAJORITY | ACCGCACCTTCTTCGCCCTGAAGGGCCTCACCAACCOCGGGGGAACCGGTGCAGGGCGTCTACGGCCTT | |
| DNAPTAQ |CA.....G.G..... | 140 |
| DNAPTFL |T.....C.....C.T..... | 137 |
| DNAPTTH |G..... | 140 |
| MAJORITY | CGCCAAGAGCCTCCTCAAGGCCCTGAAGGAGGACGGGGACXXGCCGGTGXTCGTGGTCTTTGACGCCAAG | |
| DNAPTAQ |C.....A..... | 207 |
| DNAPTFL |A.....GT.T..... | 204 |
| DNAPTTH |T.AA..C..CT..... | 280 |
| MAJORITY | GCCCCCTCCTTCGGCCACGAGGCCTACGAGGCCTACAAGCGGGCCGGGCCCCACCCCGGAGGACTTTC | |
| DNAPTAQ |G..GG.....G..... | 277 |
| DNAPTFL | | 274 |
| DNAPTTH |GA.....G.....C.....C..... | 280 |
| MAJORITY | CCCGGCAGCTCGCCCTCATCAAGGAGCTGGTGACCTCCTGGGGCTTGCGCGCCTCGAGGTCCCCGGCTA | |
| DNAPTAQ |A.....G.....G..... | 347 |
| DNAPTFL |G.....T.....A.C.....T..G..G.....T..... | 344 |
| DNAPTTH | | 350 |

FIG. 2A

MAJORITY CGAGCGGACGACGTCTGGCCACCTGGCCCAAGAGCGGAAAGGAGGGTACGAGGTGCGCATCCTC
 DNAPTAQC.....G.....C.....C..... 417
 DNAPTFL T.....G.....CG..... 414
 DNAPTTHT.C..... 420

MAJORITY ACCGCCGACCGGACCTCTACCGCTCTTCCGACCGCATCGCCGTCTCCACCCCGAGGGGTACCTCA
 DNAPTAQAAA.....T.....CA..... 487
 DNAPTFL ..T.....G.G.....A.....T.....G. 484
 DNAPTTHA.G.C.....G.....CC..... 490

MAJORITY TCACCCCGCGGTGGCTTTGGGAGAAAGTACGGCCTGAGGCCGGAGCAGTGGTGGACTACCGGGCCCTGGC
 DNAPTAQC.....A.....C.C.....CC.....A. 557
 DNAPTFLAC.....C.C.....T.C.....C.T 554
 DNAPTTHA.....C.....T.C.....C.T 560

MAJORITY GGGGGACCCCTCCGACAACCTCCCCGGGTCAAGGGCATCGGGGAGAAAGACCGCCXGAAGCTCCTCXAG
 DNAPTAQ C.....GAG.....T.....G..GAG.....T..GG.. 627
 DNAPTFLG..T..A.....G.....A..G...A..CGC 624
 DNAPTTHA.....TC.....A.. 630

MAJORITY GAGTGGGGAGCCTGGAAACCTCCTCAAGAACCTGGACCGGGTGAAGCCCGC...CXTCCGGGAGAAGA
 DNAPTAQGC.....C.....A..... 694
 DNAPTFLT.C.C.....A.....T.....T.G.....C 691
 DNAPTTHA.....A.....A.AAA.G..... 700

FIG. 2B

| | | |
|----------|---|------|
| MAJORITY | TCCAGGGCCACATGGAXGACCTGAXGCTCTCCTGGGAGCTXTCCAGGTGCGCACCGACCTGCCCTGGA | |
| DNAPTAQ |T.....C..T.....A.....C..GG..A..... | 764 |
| DNAPTFL |GGG.....G..C.....GCC..T.....C..A.....T.....A...T..... | 761 |
| DNAPTTH |A.....C.....A.....C..G.....T.....C.....G.....C..... | 770 |
| MAJORITY | GGTGGACTTCGCCAAGXGGCGGGAGCCCGACCGGGAGGGGCTTAGGGCCTTTCTGGAGAGGCTGGAGTTT | |
| DNAPTAQ |AA.....AA.....A.....A..... | 834 |
| DNAPTFL |GG..G..C..C..CACA...A...T.....T...GC...T...T...C...T..... | 831 |
| DNAPTTH |C.....C..G.....C.....C.....C..... | 840 |
| MAJORITY | GGCAGCCTCCTCCACGAGTTCGGCCTCCTGTGAGGGCCCCCAAGGCCCTGGAGGAGGCCCTGCCCCCCCGC | |
| DNAPTAQ |T.....T.....AA..... | 904 |
| DNAPTFL |A.....G.....G.....G...G...GGCA.....T... | 901 |
| DNAPTTH |C.....C.....GCCC..... | 910 |
| MAJORITY | CGGAAGGGGCTTCGTGGGCTTTGTCTCTTCCCGCCCCCGAGCCCATGTGGGCCGAGCTTCTGCCCTGGC | |
| DNAPTAQ |G.....G.....AAG.....T..... | 974 |
| DNAPTFL |T..TT.....TC..T.....T..... | 971 |
| DNAPTTH |C.....C.....G.....AAA..... | 980 |
| MAJORITY | CGCCGCCAGGGAGGGCGGGTCCACCGGGCACCGACCCCTTTAXGGGCCTXAGGGACCTXAAGGAGGTG | |
| DNAPTAQ |G.....C..C..G..T.A..AA.C...C.....G.....C... | 1044 |
| DNAPTFL | T.GG..GT.....G..CC...T.....A.....C...G.....G.....T...G.... | 1041 |
| DNAPTTH |TG.....C.....G.....G.....G.....G.....G.....C.....C..... | 1050 |

FIG. 2C

| MAJORITY | CGGGGXCTCCTCGCCCAAGGACCTGGCCGTTT | TGGCCCTGAGGGAGGGCCTXGACCTCXTGCCCCGGGGACG |
|----------|--|--|
| DNAPTAQ | ...G..T... | ...A...AG...C...A...T.G...CC...C... |
| DNAPTFL | ...AA...G... | ...G...C...G...T.C..A.A... |
| DNAPTTH | ...C...C...C... | ...TC...G..A...G...G... |
| MAJORITY | ACCCCATGCTCCTCGCCTACCTCCTGTGACCCCTC | CAACACACCCCGAGGGGGTGCCCCGGCGCTACGG |
| DNAPTAQ | ...G...T... | ...T... |
| DNAPTFL | ...G...T... | ...T...T... |
| DNAPTTH | ...G...T... | ...G...G... |
| MAJORITY | GGGGGAGTGGACGGAGGAXGCGGGGGAGCGGGCCCTCCT | XTCCGAGAGGCTCTTCCXGAACCTXXXGGAG |
| DNAPTAQ | C...G...G... | ...GC...T...GCC...GTG..G. |
| DNAPTFL | ...T...A... | ...GG...C.C...A..C...AAA... |
| DNAPTTH | ...C..C.CCC.C... | ...C.G...CAT.G...CCTTA.. |
| MAJORITY | CGCCTTGAGGGGAGGAGGCTCCTTTGGCTTTACCAGGAGGTG | GAGAGCCCTTTCCCGGGTCCIGG |
| DNAPTAQ | A.G... | ...G...G...GCT... |
| DNAPTFL | ...A...A..A.C.C.G... | ...G...G...GT... |
| DNAPTTH | ...C...A...A...C...C... | ...A...C...C... |
| MAJORITY | CCCACATGGAGGCCACGGGGGTXXCGGCTGGACGTGGCCT | TACCTCCAGGCCCTXTCCCTGGAGGTGGCGGA |
| DNAPTAQ | ...GG... | ...G..C...T..AG...T.G...C... |
| DNAPTFL | ...C...C... | ...C...C...A..C |
| DNAPTTH | ...C...A...A...T... | ...T...C.T... |

FIG. 2D

| | | |
|----------|--|------|
| MAJORITY | GGAGATCCGCCGCTCGAGGAGGAGGTCTTCCGCCTGGCCGGCCACCCCTTCAACCTCAACTCCCGGGAC | |
| DNAPTAQ |GC.....CC..... | 1464 |
| DNAPTFL |G.G....AG..G..... | 1461 |
| DNAPTTH |T.....G..... | 1470 |
| MAJORITY | CAGCTGGAAAGGGTGCTCTTTGACGAGCTXGGGCTTCCCGCCATCGGCAAGACGGAGAAGACXGGCAAGC | |
| DNAPTAQ |C.....A..... | 1534 |
| DNAPTFL |GC.....G.C..G..T..... | 1531 |
| DNAPTTH |TA.....T.G..G.....C.A..... | 1540 |
| MAJORITY | GCTCCACACGCGCCGCTGCTGGAGGCCCTXCGXGAGGCCACCCCATCTGCTGGAGAAGATCCTGCAGTA | |
| DNAPTAQ |C.....C..C..... | 1604 |
| DNAPTFL |T.....G..A.....CCGC..... | 1601 |
| DNAPTTH |G.....A..G.....C...C..... | 1610 |
| MAJORITY | CCGGGAGCTCACCAAGCTCAAGAACACCTACATXGACCCCTGCCXGXCTCTGTCACCCAGGACGGGC | |
| DNAPTAQ |G.....G.....T.....G.A....A..... | 1674 |
| DNAPTFL |A.....A.....C.C...G.....A..C... | 1671 |
| DNAPTTH |G.G.....AAG.....G..... | 1680 |
| MAJORITY | CGCCTCCACACCCGCTTCAACCAGACGGCCACGGCCACGGGACGGCTTAGTAGCTCCGACCCCAACCTGC | |
| DNAPTAQ |A.....T.....C..... | 1744 |
| DNAPTFL |G.....C.....TCC..... | 1741 |
| DNAPTTH |G.....G..... | 1750 |

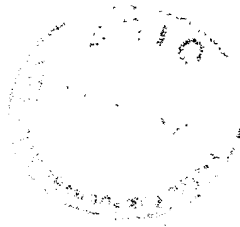
FIG.2E

| | | |
|----------|---|------|
| MAJORITY | AGAACATCCCCGTCCGCACCCXCTGGGCCAGAGGATCCGCCGGGCTTCGTGGCCGAGGAGGGXTGGGT | |
| DNAPTAQ |G..T..G.....A.C.....G....C.. | 1814 |
| DNAPTFL |G.....T.....C.C.....A.....C..... | 1811 |
| DNAPTTH |CT.....C.....T.....C..... | 1820 |
| MAJORITY | GTTGGTGGCCCTGGACTATAGCCAGATAGAGCTCCGGGTCTCGGCCACCTCTCCGGGGACGAGAACCTG | |
| DNAPTAQ | A.....A.....A.....G.....C..... | 1884 |
| DNAPTFL |T.T.....C.....T.....T..... | 1881 |
| DNAPTTH |C.....C.....C.....A..... | 1890 |
| MAJORITY | ATCCGGGTCTTCCAGGAGGGAGGACATCCACACCCAGACCGCCAGCTGGATGTTCCGGCGTCCCCCGG | |
| DNAPTAQ |C.....C.....GG.....G.... | 1954 |
| DNAPTFL |T.....T.....T.....TT....C.. | 1951 |
| DNAPTTH |A.....A.....A..... | 1960 |
| MAJORITY | AGGCCGTGGACCCCTGATGCGCCGGCGGCCCAAGACCATCAACTTCGGGGTCTCTACGGCATGTCGGC | |
| DNAPTAQ |A.GG..A.....T.....GG.G.....G.... | 2024 |
| DNAPTFL |A.GG..A.....T.....GG.G.....G.... | 2021 |
| DNAPTTH |A.GG..A.....T.....GG.G.....G.... | 2030 |
| MAJORITY | CCACCGCCTCTCCAGGAGCTTGCCCATCCCTACGAGGAGGGGTGGCCTTCATTGAGCGCTACTTCCAG | |
| DNAPTAQ |A.....A.....T.....CCA.....T.... | 2094 |
| DNAPTFL |GG.....T.....T..... | 2091 |
| DNAPTTH |TA.G.....T.....A.....A 2100 | |

FIG. 2F

| | | |
|----------|---|------|
| MAJORITY | AGCTTCCCAAGGTGCGGCTGGATTGAGAAGACCCCTGGAGGAGGCGCAGGAGGGGTACGTGGAGA | |
| DNAPTAQ | | 2164 |
| DNAPTFL | ...A.....GG.....C.....C.CC.....T..... | 2161 |
| DNAPTTH |A.A.....G.....A.....C.....A. | 2170 |
| MAJORITY | CCCTCTTCGGCCGCGGCTACGTGCCCGACCTCAACGCCCGGGTGAAGAGCGTGCGGGAGGCGGCGGA | |
| DNAPTAQ |C.....A.....AG.G.....C..... | 2234 |
| DNAPTFL |T.....C..... | 2231 |
| DNAPTTH | ...AA.AA.....CA.....C..... | 2240 |
| MAJORITY | GCGCATGGCCTTCAACATGCCCCGTCCAGGGCACCGCCGCCGACCTCATGAAGCTGGCCATGGTGAAGCTC | |
| DNAPTAQ |G.....T..... | 2304 |
| DNAPTFL |G.....CG...T | 2301 |
| DNAPTTH |C..... | 2310 |
| MAJORITY | TTCCCCCGGCTXCAGGAAATGGGGGCCAGGATGCTCCTXCAGGTCCACGACGAGCTGGTCCTCGAGGCC | |
| DNAPTAQ |A...GG.....T..... | 2374 |
| DNAPTFL |T.....C.....TT.G.....G..... | 2371 |
| DNAPTTH |C..C.G...G.....C.C.....CC...G..... | 2380 |
| MAJORITY | CCAAAGAGCGGGCGGAGGXGGTGGCCGCTTTGGCCAAAGAGGTCTATCCCTGGCCGT | |
| DNAPTAQ | .A.....A.....CC.....CGGC.....G..... | 2444 |
| DNAPTFL | ...G.C.....AG...A.....GG.....CAG.. | 2441 |
| DNAPTTH | .C...C.....C...A.....G.....C.....AA..C.....C..... | 2450 |

FIG. 2G



| | | |
|----------|--|------|
| MAJORITY | GCCCCCTGGAGGTGGAGGTGGGGGATGGGGGAGGACTGGCTCTCCGCCCAAGGAGTAG | |
| DNAPTAQ |A.....GA | 2499 |
| DNAPTFL |CC..... | 2496 |
| DNAPTTH |T.....GT... | 2505 |

FIG.2H

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MAJORITY MXAMLPLFEPKGRVLLVDGHHLAYRTFFALKGLTTSRGEVPQAVYGFAKSLLKALKEDG·DAVXVVVFDK
TAD PR0 .RG.....H.....I.....69
TFL PR0 .....V.V.....68
TTH PR0 .E.....YK..F.....70

MAJORITY APSFRHEAYEAYKAGRPTPEDFPROLALIKELVDLLGLXRLEVPGYEADDVLATLAKAEKEGYEVRI
TAG PR0 .....GG.....A.....S.....139
TFL PR0 .....V.....F.....R.....138
TTH PR0 .....FT.....140

MAJORITY TADRDLYQLLSDRIAVLHPEGYLITPAWLWEKYGLRPEQWVDYRALXGDPNDLPGVKGIGECTAXKLLX
TAG PR0 .....K.....H.....D..A.....T..E.....R...E 209
TFL PR0 .....E...I.....Y.....A.....I.....QR..IR 208
TTH PR0 .....V...V.....H...E.....F..V.....L...K 210

MAJORITY EWGSLENLLKNLDRVKP·XXREKIXAHMEDLXLSXXLSXVRTDLPLEVDFAXRREPDRGLRAFLERLEF
TAG PR0 .....A.....L...L...D..K..WD.AK.....K.....R.....278
TFL PR0 .....FQH...Q...SL...LQ.G..A.A..RK..Q.H.....GR..T.NL.....277
TTH PR0 .....ENV...K..L...R..LE..R.....L.QG.....280

MAJORITY GSLLHEFGLLEXPKALEEAPWPPPEGAFVGFVLSRPEPMWAEELLALAAARXGRVHRAXDPLXGLRDLKEV
TAG PR0 .....S.....K.....D.....PE.YKA.....A 348
TFL PR0 .....G...A.....L..SF.....G.WE..L...Q...R.....G. 347
TTH PR0 .....A.AP.....K.....C.D.....A..A..K..... 350

```

FIG. 3A

| | | |
|----------|--|-----|
| MAJORITY | RGLLAKDLAVLALREGDLXPGDDPMLLAYLLDPSNTTPEGVARRYGGWENTEDAGERALLSERLFXNLXX | |
| TAQ PRO |S.....G.P.....E.....A.....A.....WG | 418 |
| TFL PRO |I.....F.E.....A.....QT.KE | 417 |
| TTH PRO |S.....V.....AH.....HR...LK | 420 |
| MAJORITY | RLEGEERLLWLXYXEVEKPLSRVLAHMEATGVRLDVAYLQALSLEVAEEIRRLLEEVEFRLAGHPFNLNSRD | |
| TAQ PRO |R...R...A.....R.....A.....A..... | 488 |
| TFL PRO |K.....E.....R.....EA.V.Q..... | 487 |
| TTH PRO |K.....H.....L..... | 490 |
| MAJORITY | QLERVLFDELGLPAIGKTEKTGKRSTSAAVLEALREAHPIVEKILQYRELTKLKNITYIDPLPXLVHPRTG | |
| TAQ PRO |S.....D.I..... | 558 |
| TFL PRO |DR.....A...K... | 557 |
| TTH PRO |R...L...Q.....H.....V.....S..... | 560 |
| MAJORITY | RLHTRFNQTATATGRLSSSDPNLQNIPTPLGQRIRRAFVAEEGWXLVALDYSQIELRVLAHLSGDENL | |
| TAQ PRO |I.....L..... | 628 |
| TFL PRO |V...V..... | 627 |
| TTH PRO |A.A..... | 630 |
| MAJORITY | IRVFQEGRDIHTQTASWMFGVPPPEAVDPLMRRAAKTINFGVLYGMSAHRLSQELAIPEEAVAFIERYFQ | |
| TAQ PRO |E.....R.....Q..... | 698 |
| TFL PRO |S..G.....G..S..... | 697 |
| TTH PRO |K.....V..... | 700 |

FIG. 3B

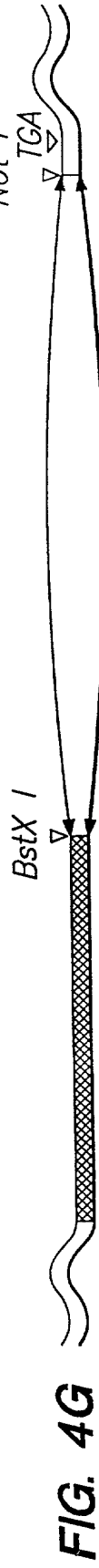
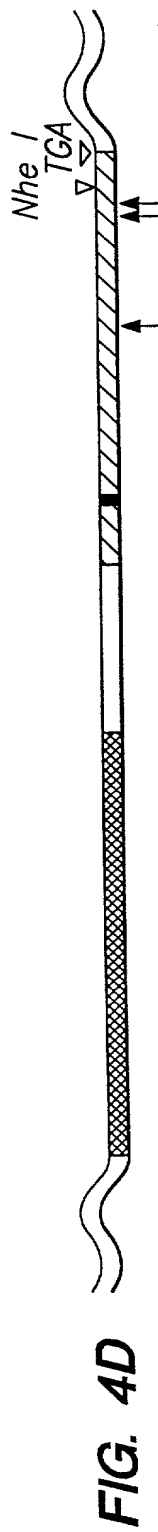
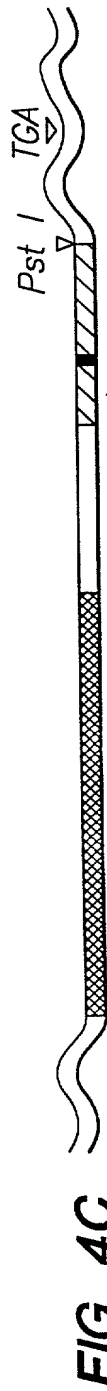
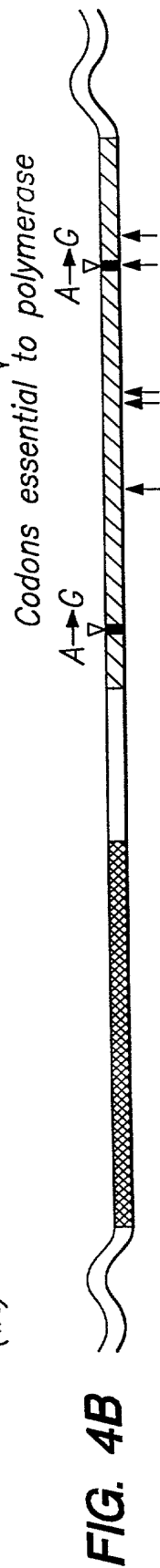
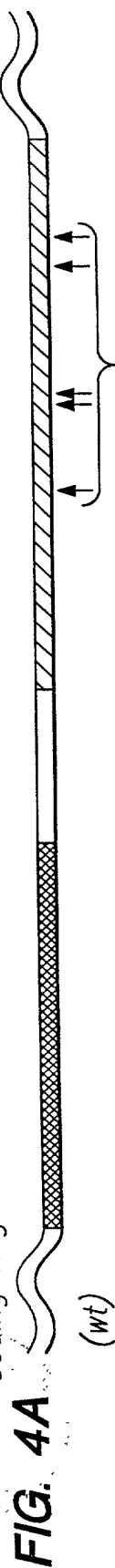
| | | | | | | | | | | | | | | | | | | | |
|----------|--------|--------|--------|--------|------|-------|------|------|-------|------|------|------|------|------|------|------|-----|----|-----|
| MAJORITY | SFPKVR | AWIEKT | LEEGRR | RGYVET | LFGR | RRYV | PD | NARV | KSVRE | AAER | MAFN | MPVQ | GTAA | DL | MKL | AMV | KL | | |
| TAQ PRO | | | | | | | | | | | | | | | | | | | 768 |
| TFL PRO | | | | | | | | | | | | | | | | | | | 767 |
| TTH PRO | | | | | | | | | | | | | | | | | | | 770 |
| | | | | | | | | | | | | | | | | | | | |
| MAJORITY | FPR | LXEM | GARM | LLQV | HDEL | VLEAP | KXRA | EXVA | ALAKE | VM | EGVY | PLAV | P | LEVE | VGXG | EDWL | SAK | EX | |
| TAQ PRO | | | | | | | | | | | | | | | | | | | 833 |
| TFL PRO | | | | | | | | | | | | | | | | | | | 831 |
| TTH PRO | | | | | | | | | | | | | | | | | | | 835 |

FIG. 3C

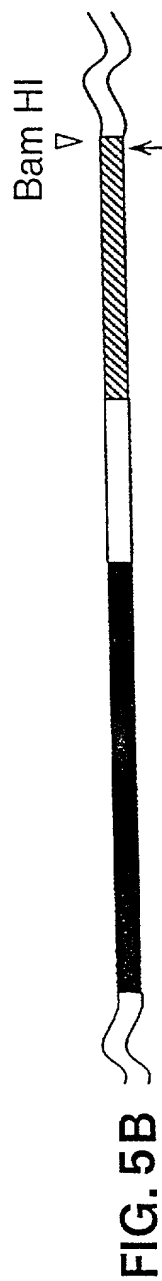
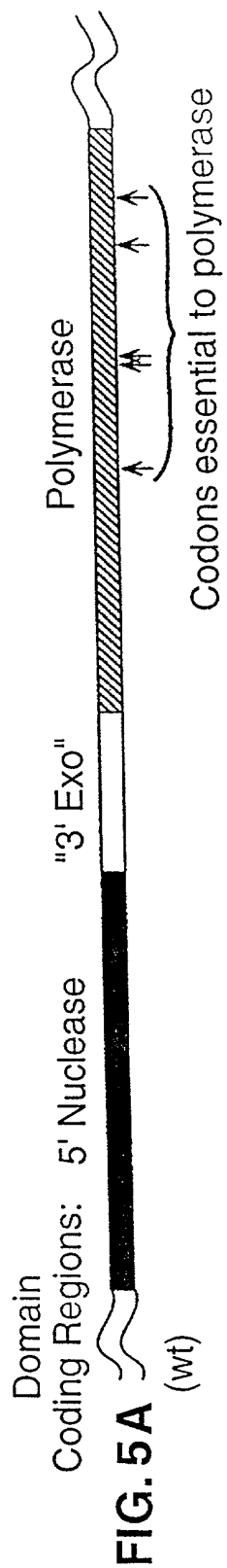
Genes for Wild-Type and Pol(-)DNAPTaq

Domain
Coding Regions: 5' Nuclease

Polymerase



Genes for Wild-Type and Pol(-)DNAPTfl



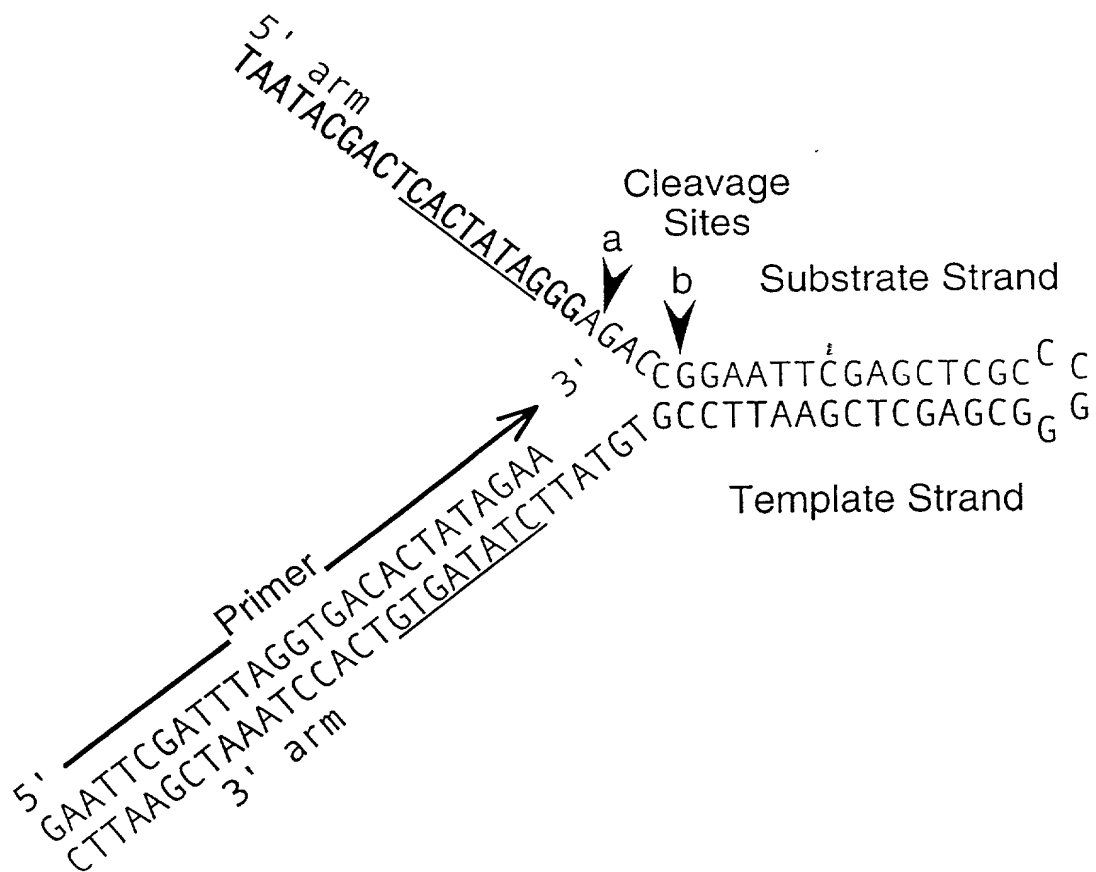


FIG. 6

10081305 .050793

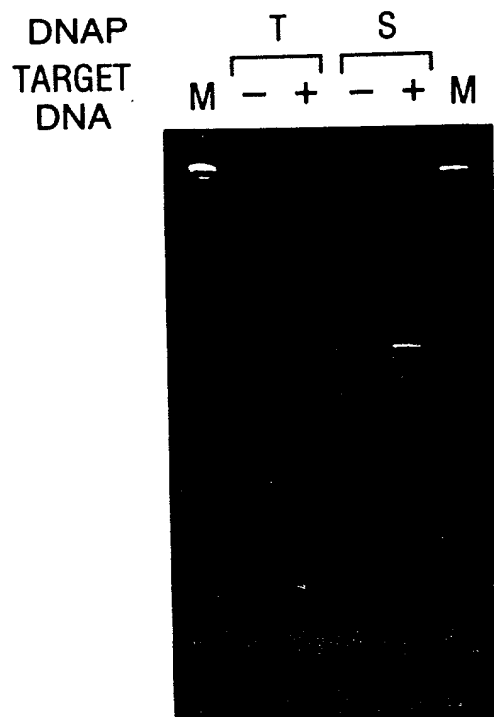


FIG. 7

10034306.060702

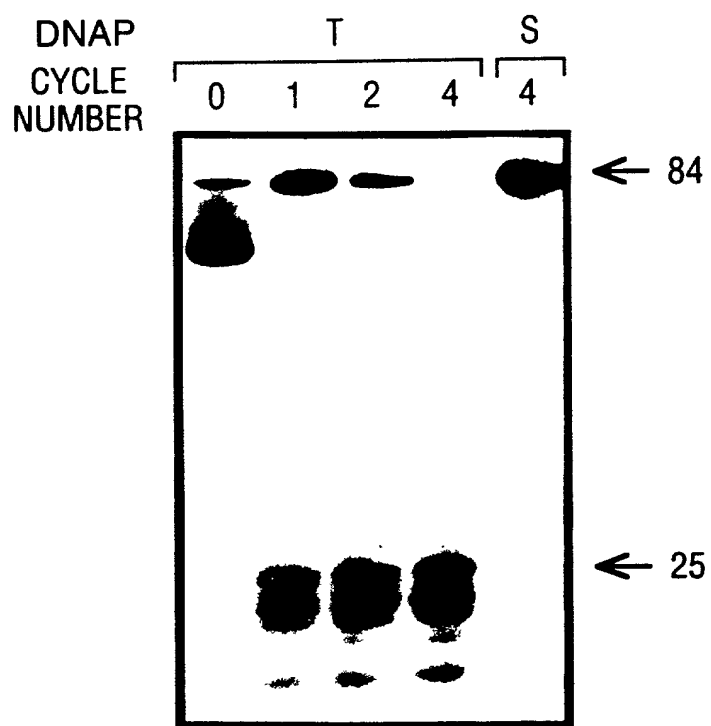


FIG. 8

| | 1 | 2 | 3 | 4 | 5 | 6 |
|---------------------|---|---|---|---|---|---|
| DNAP-T: | - | + | + | + | + | + |
| MgCl ₂ : | + | - | + | + | + | + |
| dNTPs: | + | - | + | - | + | - |
| Primers: | + | - | + | + | - | - |

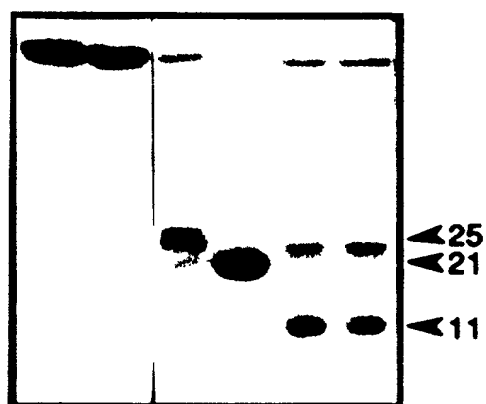


FIG. 9A

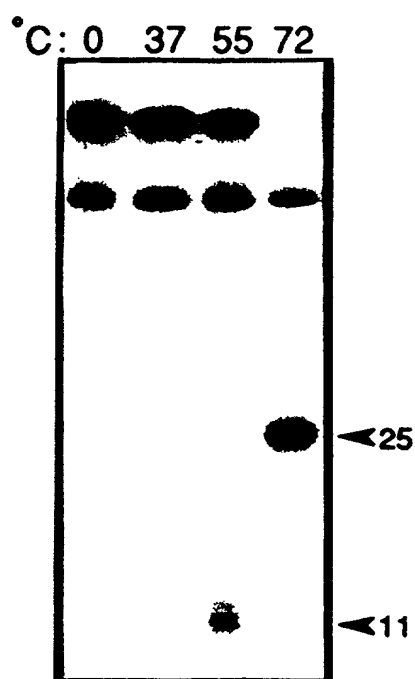


FIG. 9B

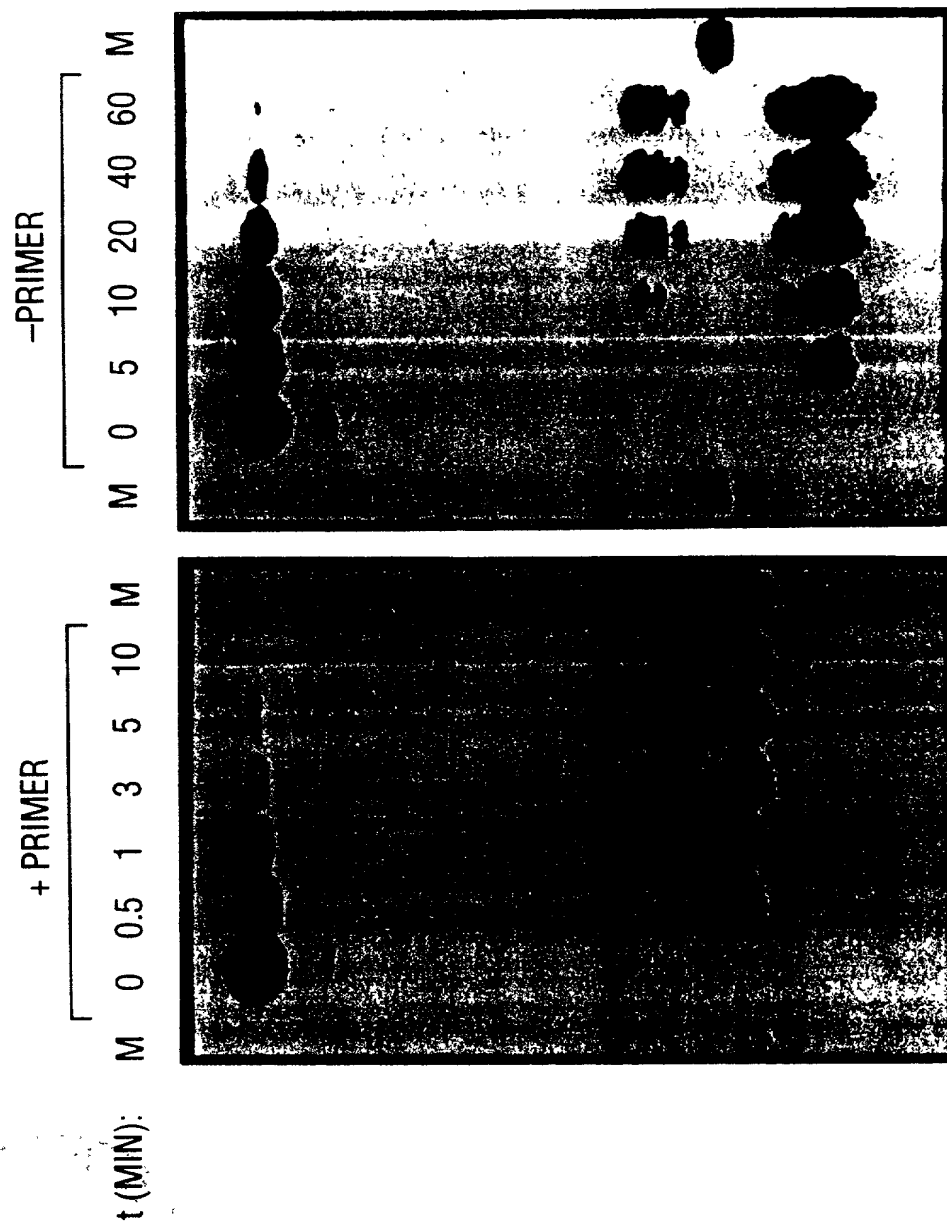


FIG. 10A

FIG. 10B

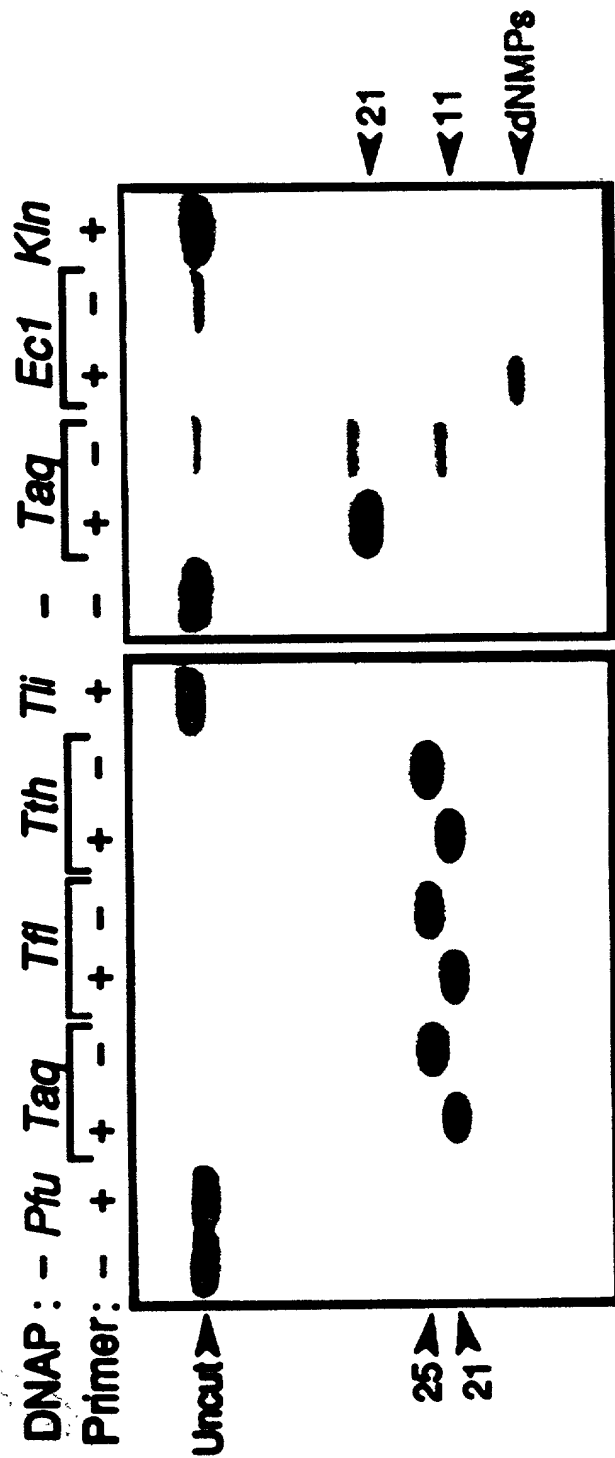


FIG. 11A

FIG. 11B

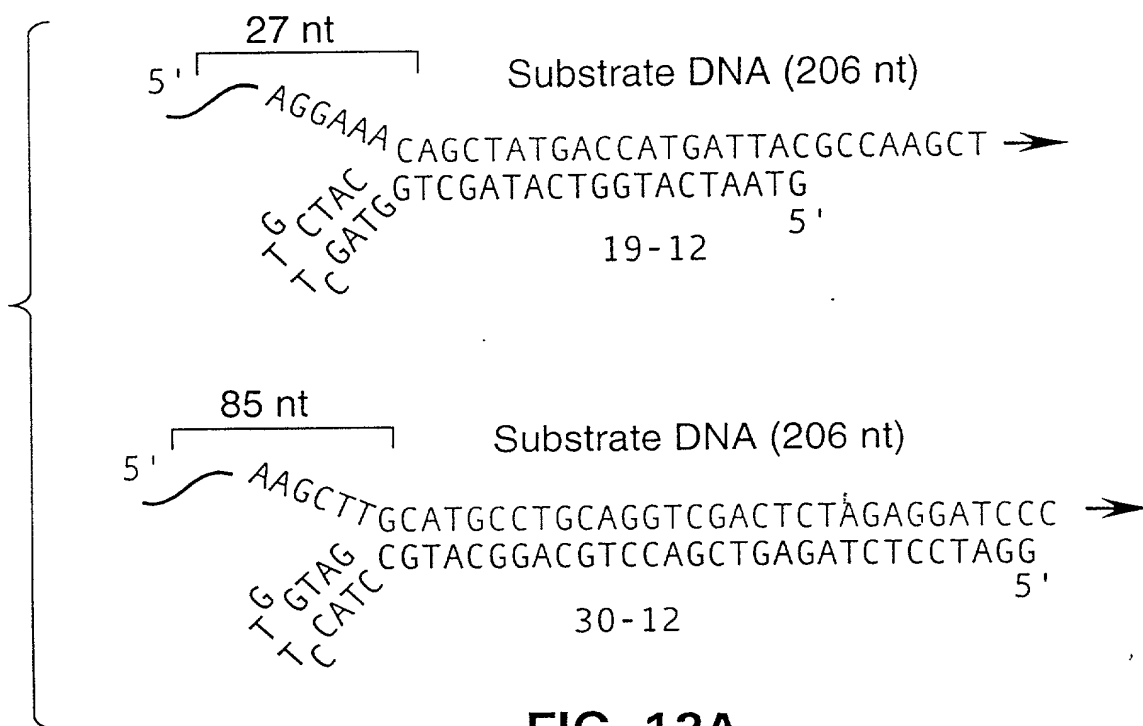


FIG. 12A

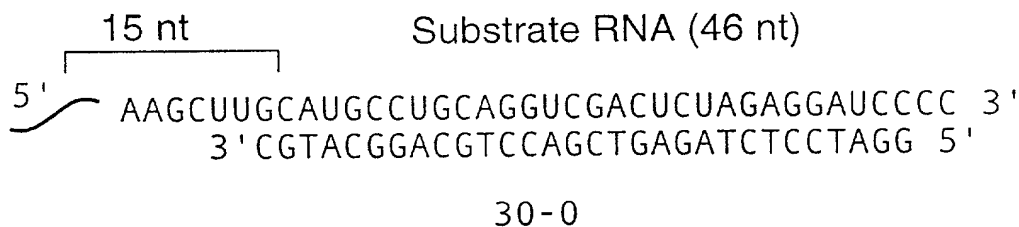


FIG. 13A

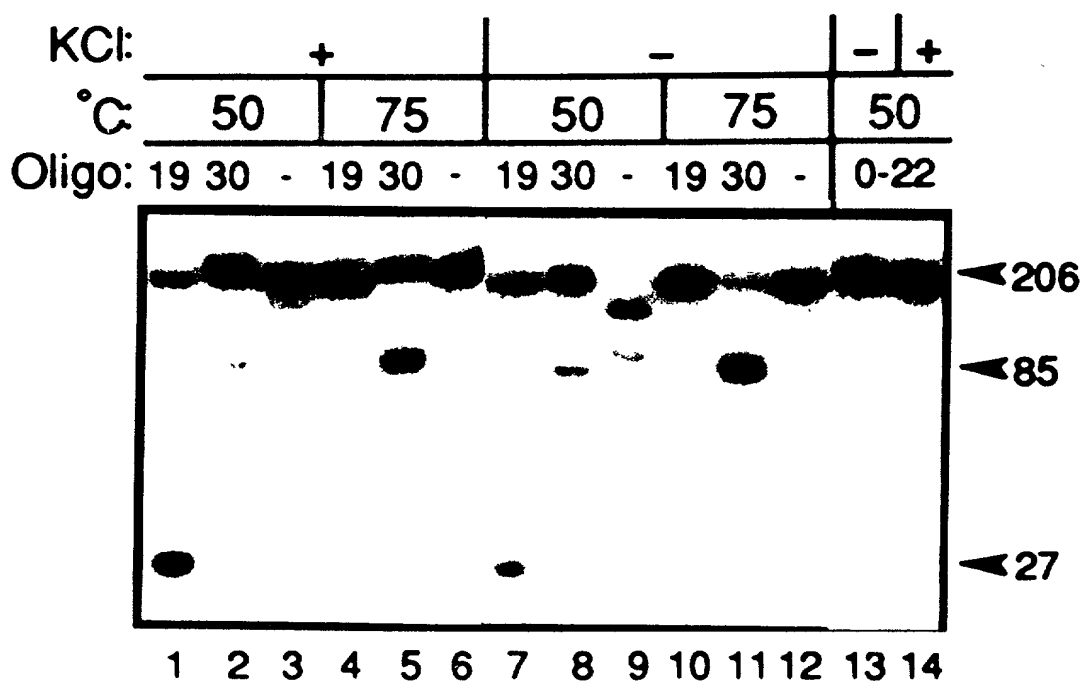


FIG. 12B

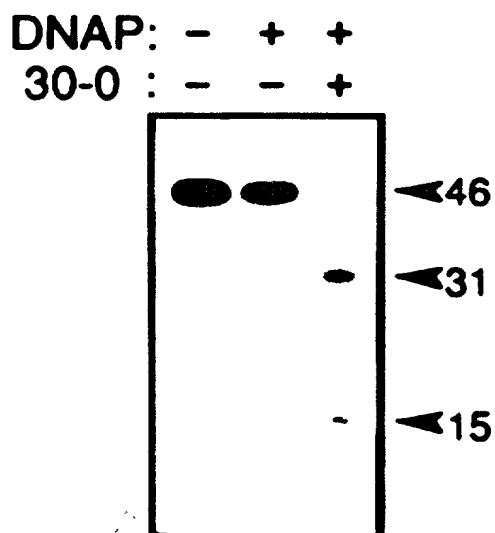
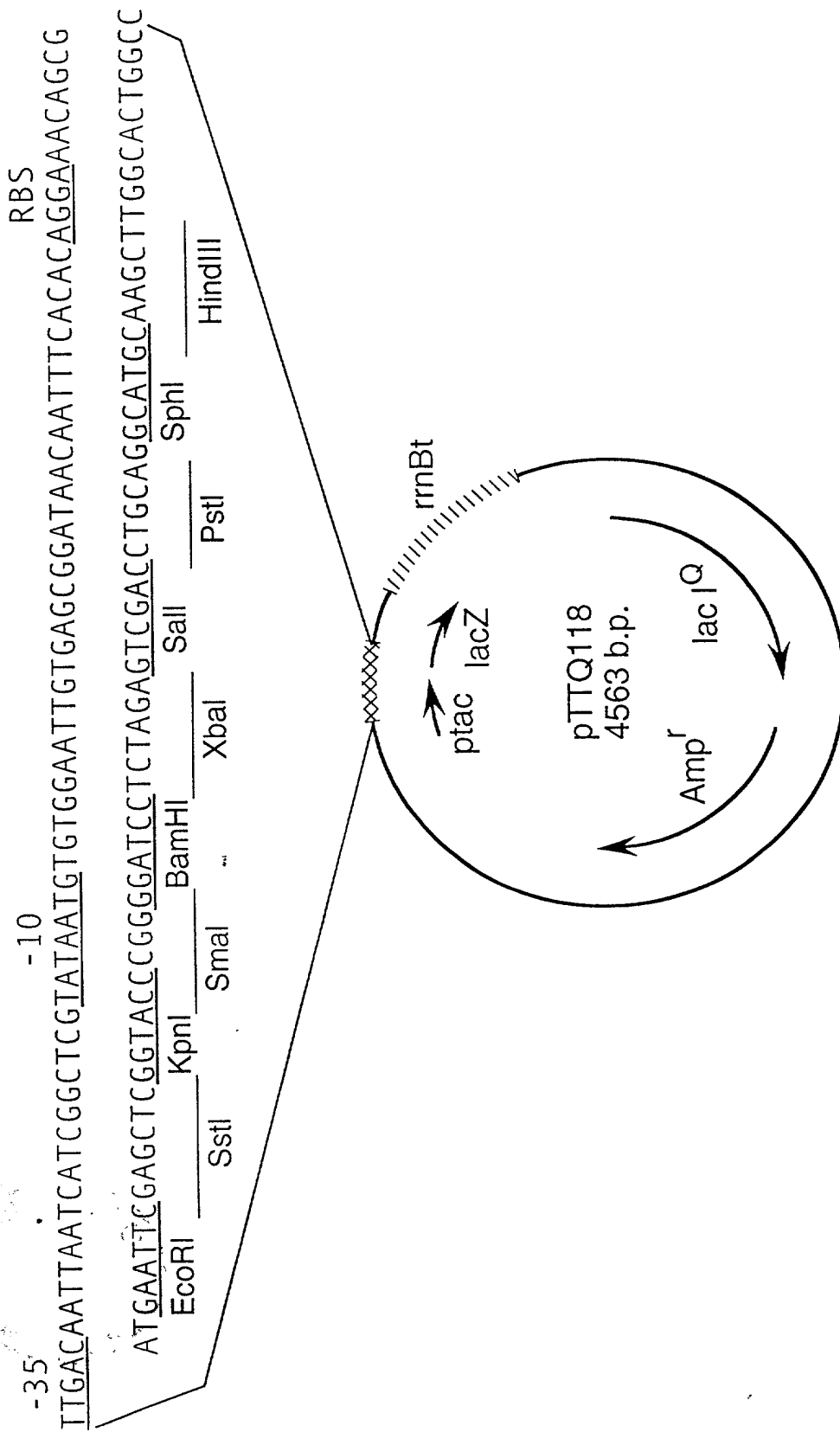
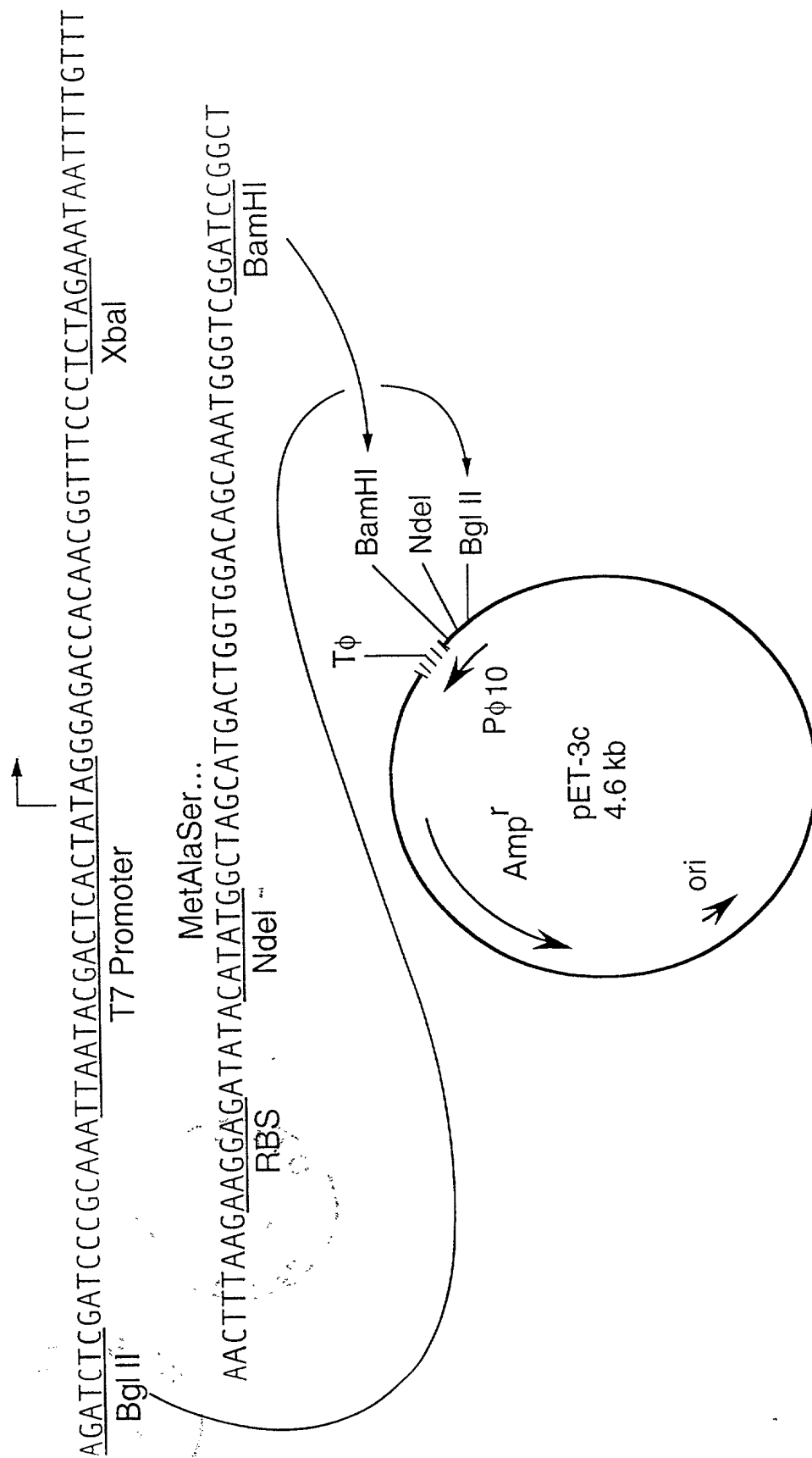


FIG. 13B



RBS: Ribosome binding site
 ptac: Synthetic tac promoter
 lac I^Q: Lac repressor gene
 lacZ: Beta-galactosidase alpha fragment
 rrnBt: E. coli rrnB transcription terminator

FIG. 14



P_{φ10}: Bacteriophage T7 $\phi 10$ promoter RBS: Ribosome binding site
T ϕ : T7 ϕ Terminator

FIG.15

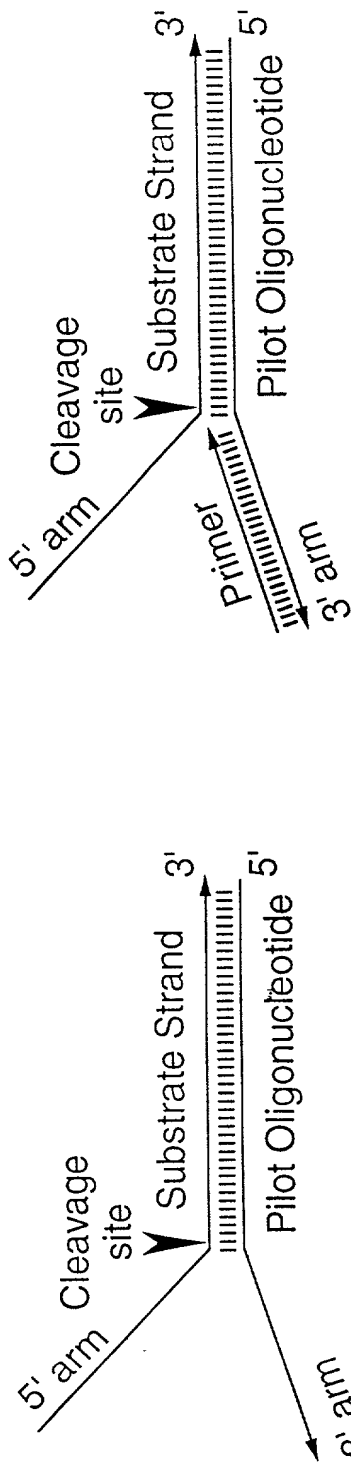


FIG. 16A

FIG. 16B

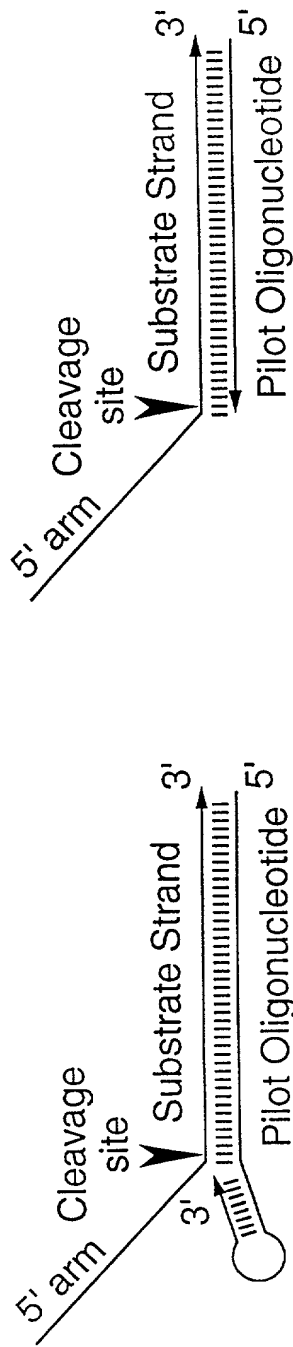


FIG. 16C

FIG. 16D



FIG. 16E

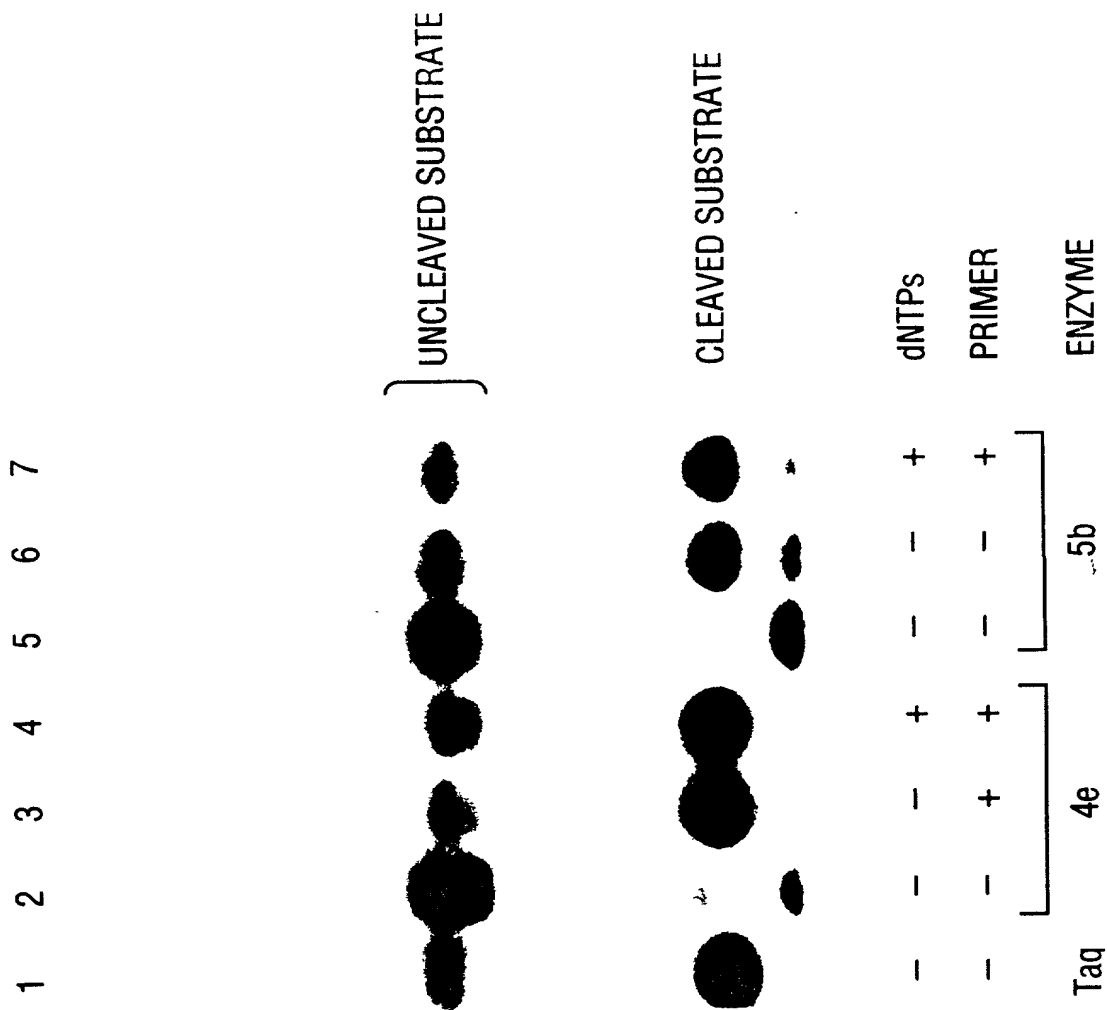


FIG. 17

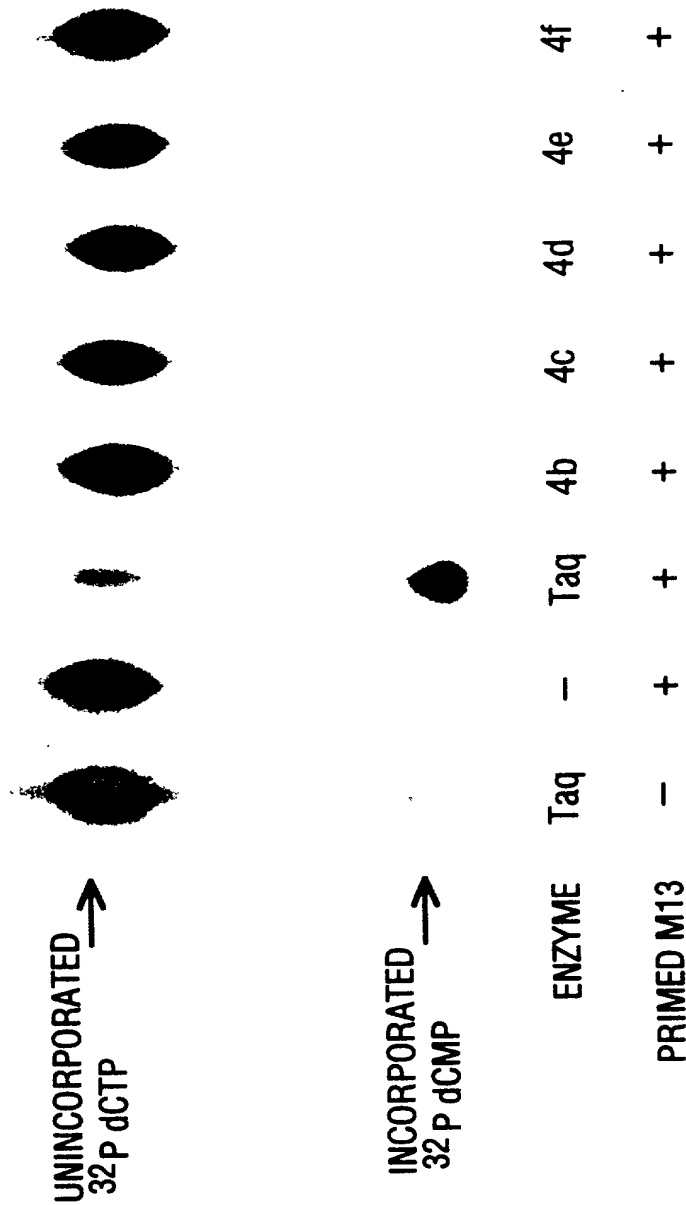



FIG. 18

(32p) 

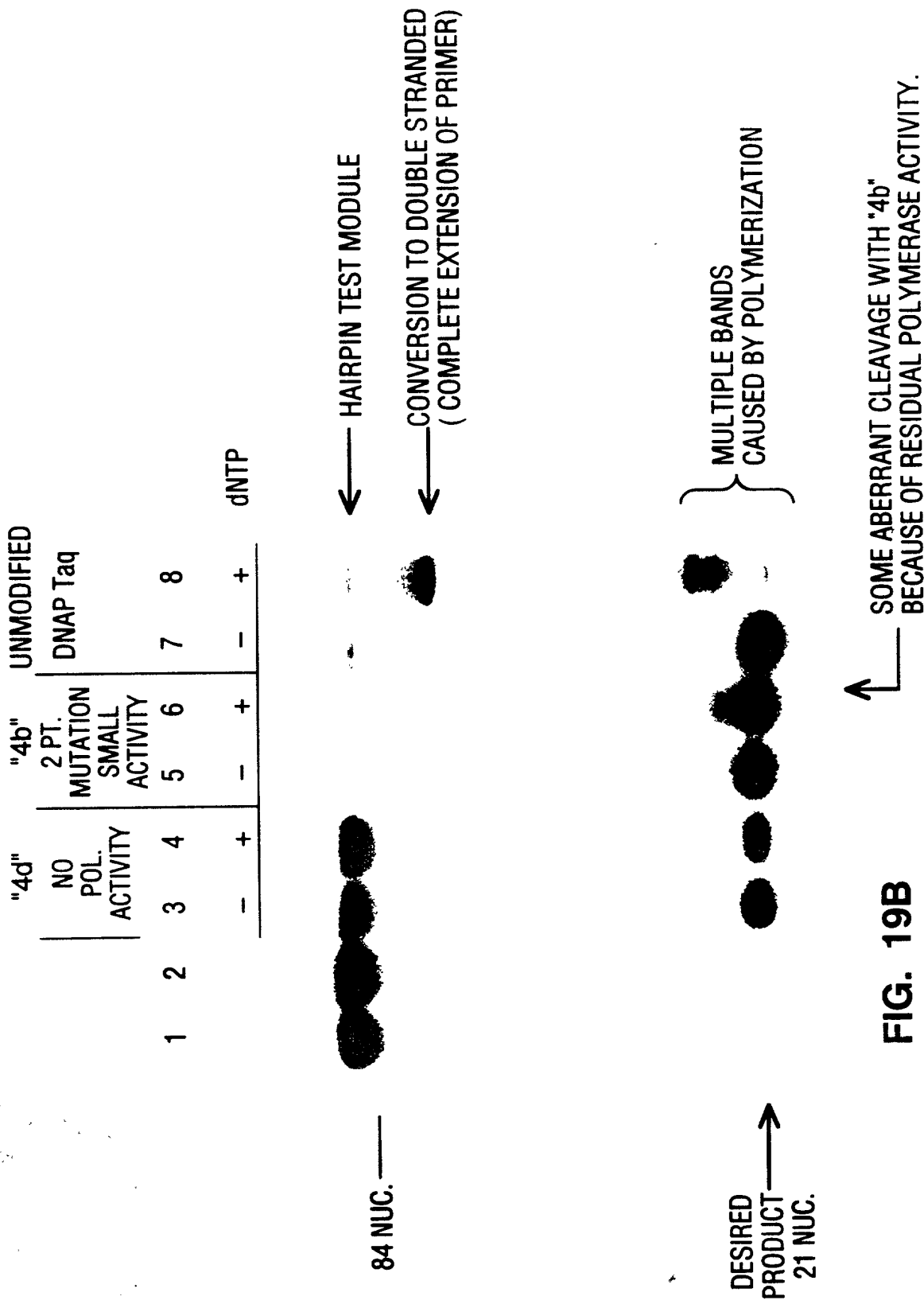


FIG. 19B

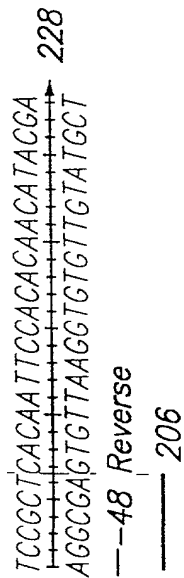
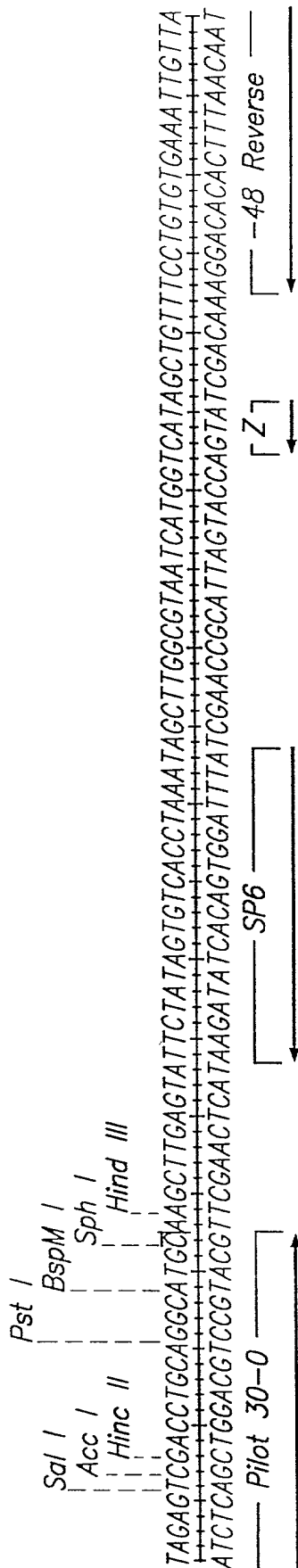
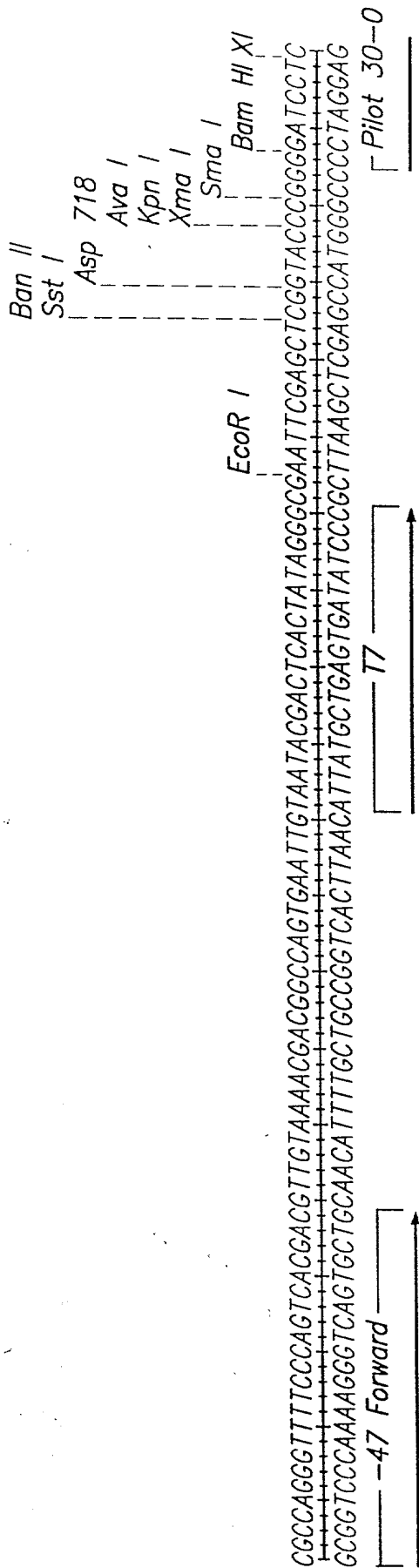


FIG. 21

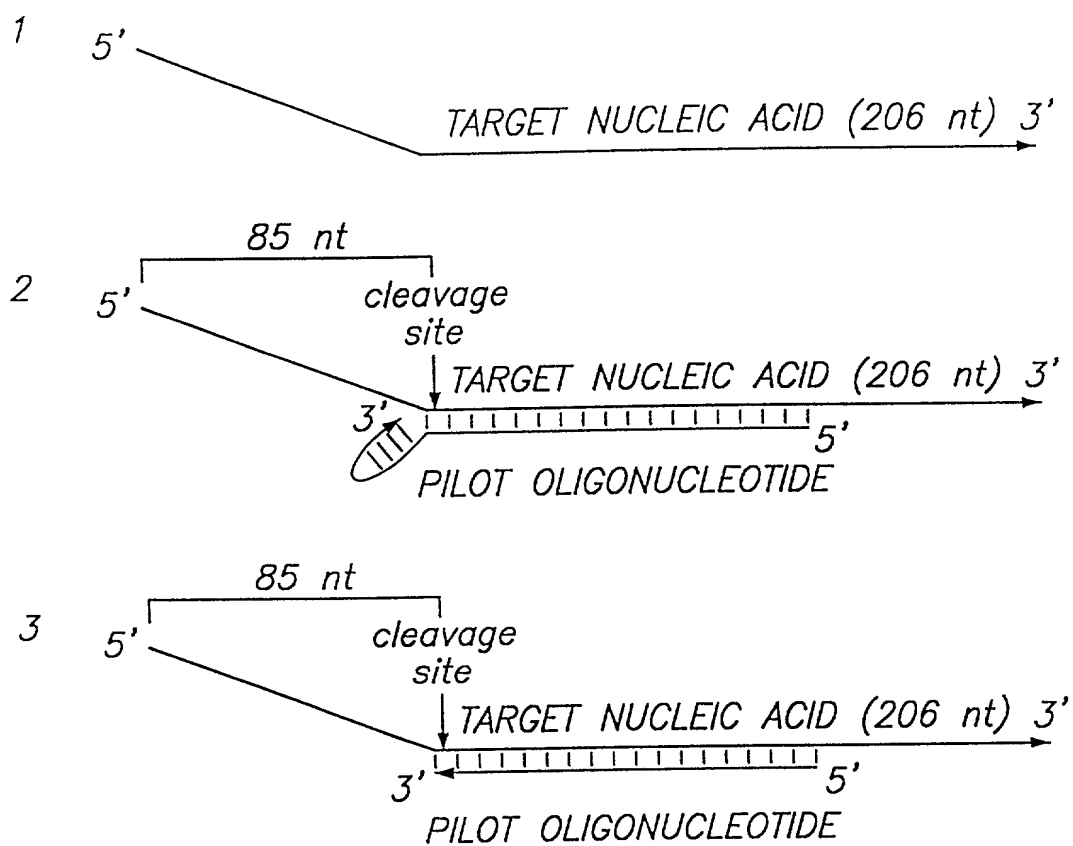


FIG. 22A

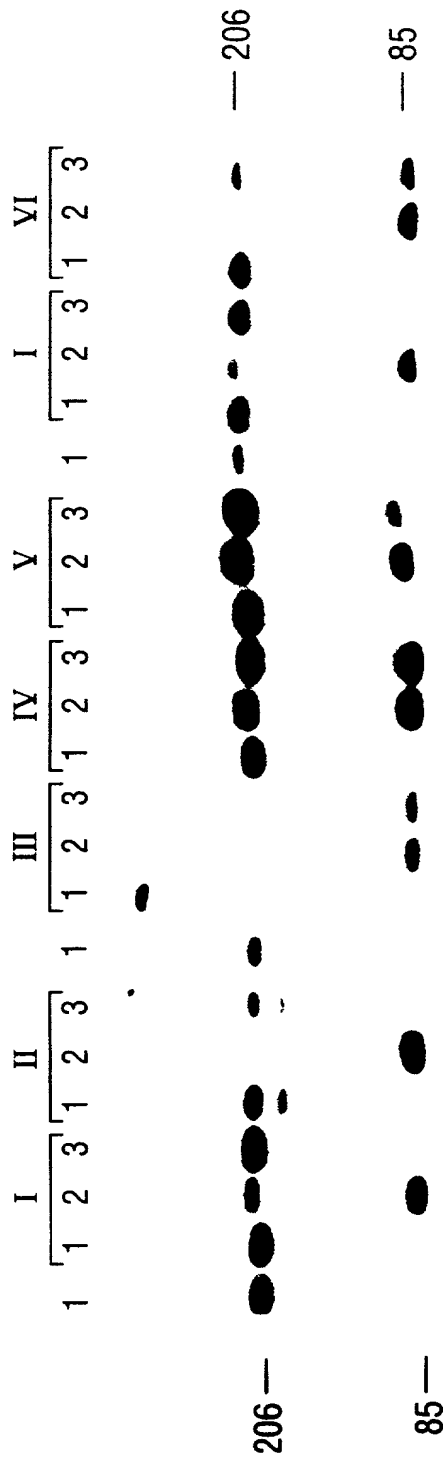


FIG. 22B

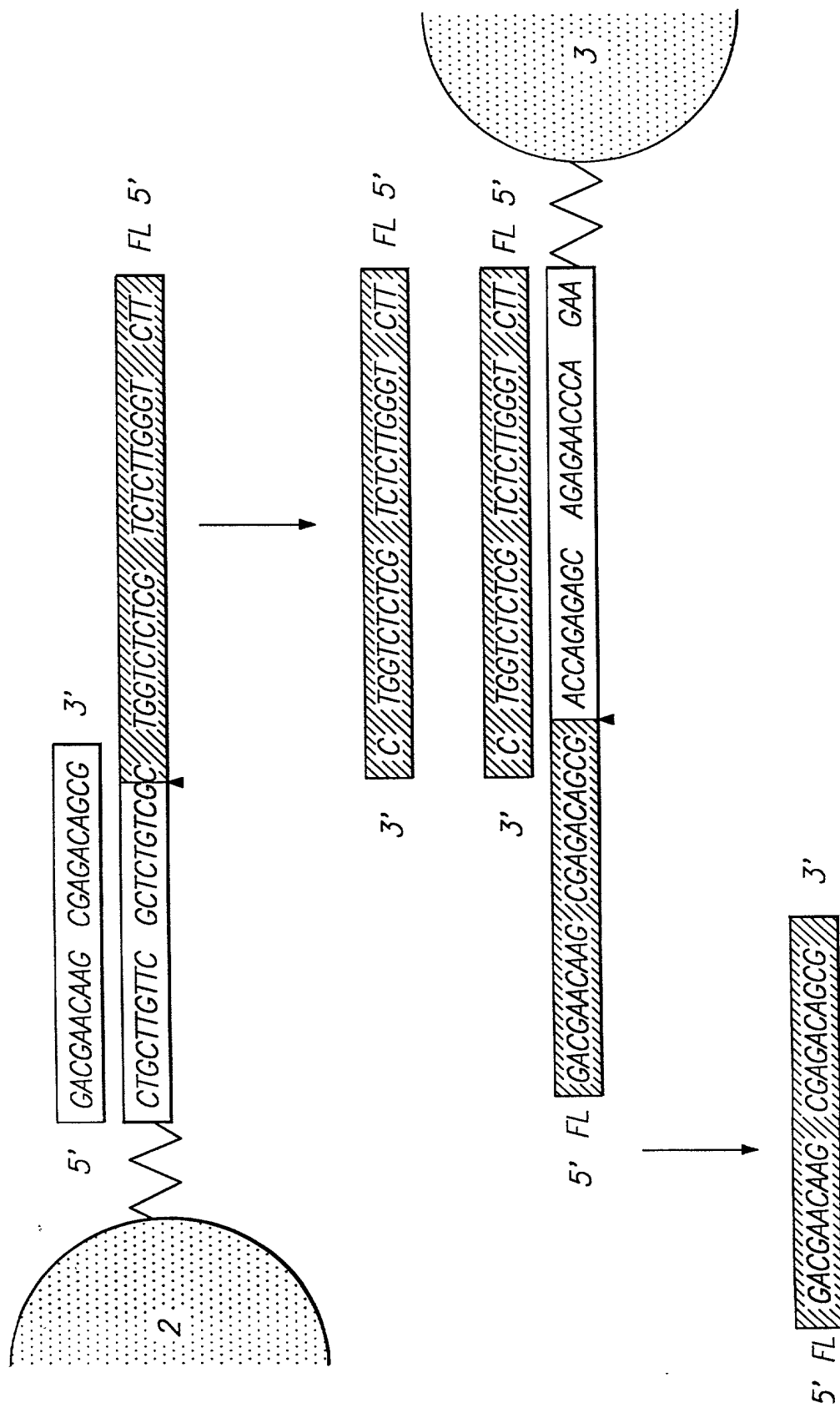


FIG. 23

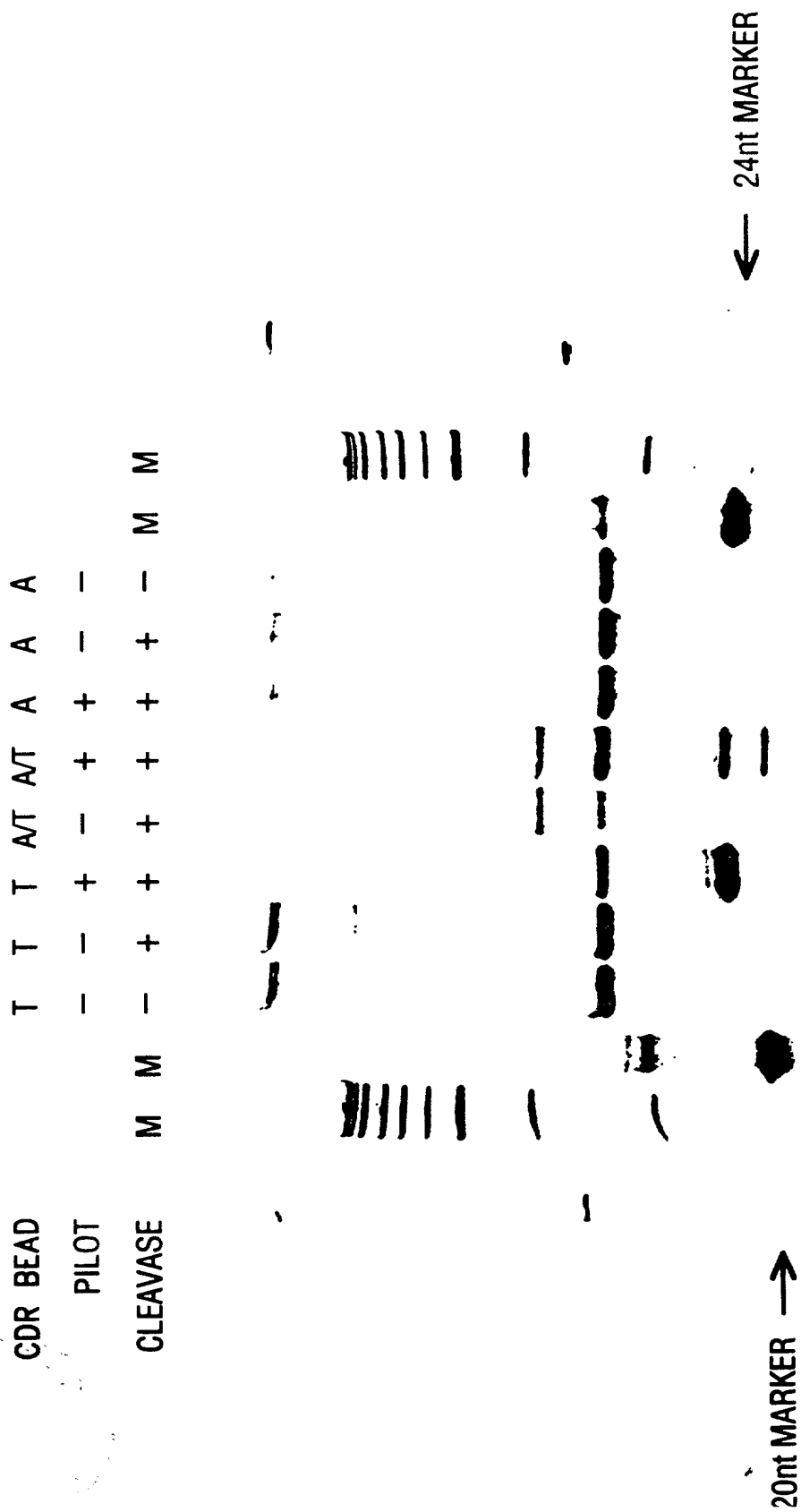


FIG. 24

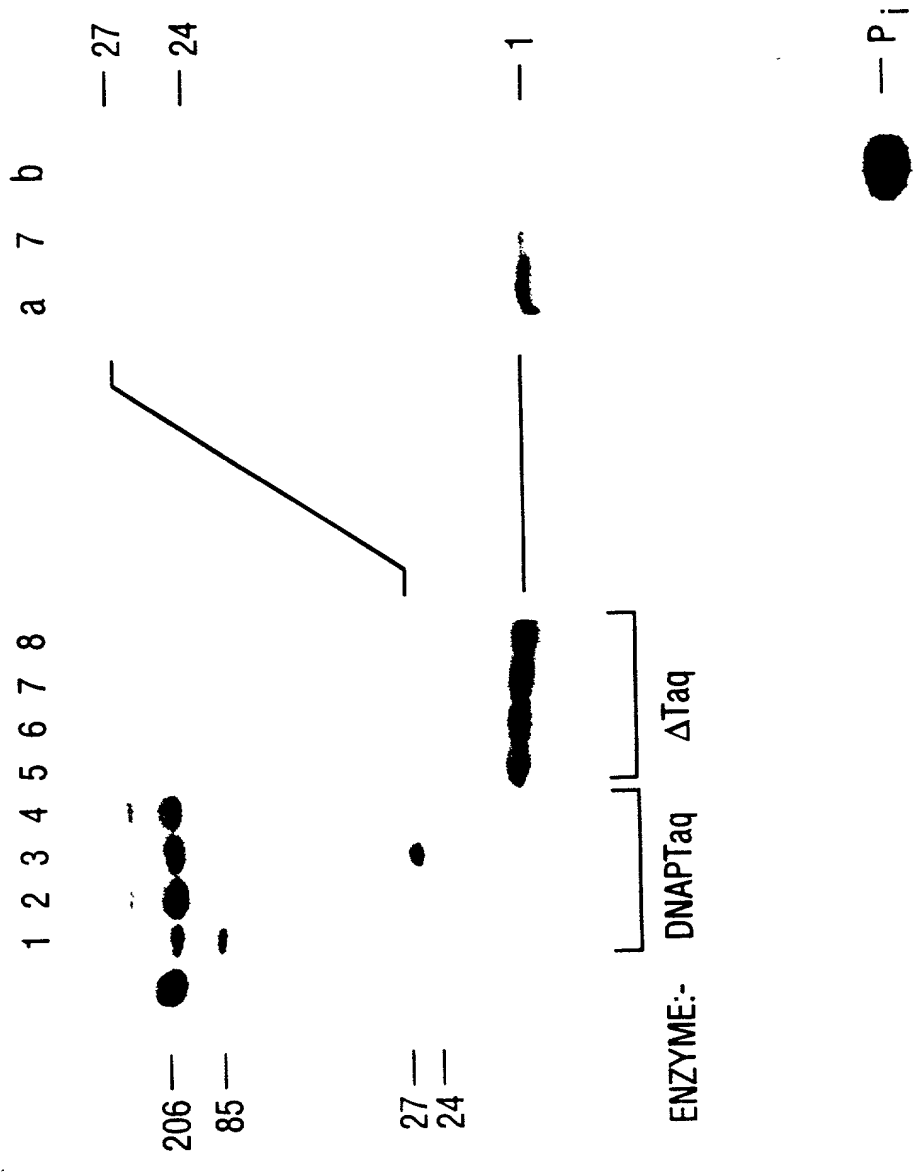
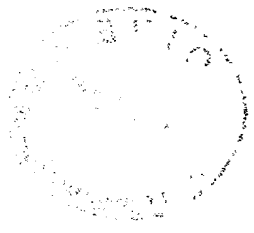


FIG. 25A

FIG. 25B

FIG. 26A

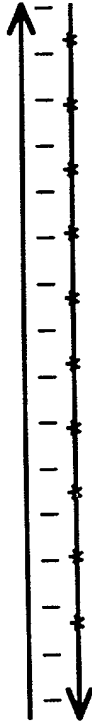


FIG. 26B

* = 32p



— 206

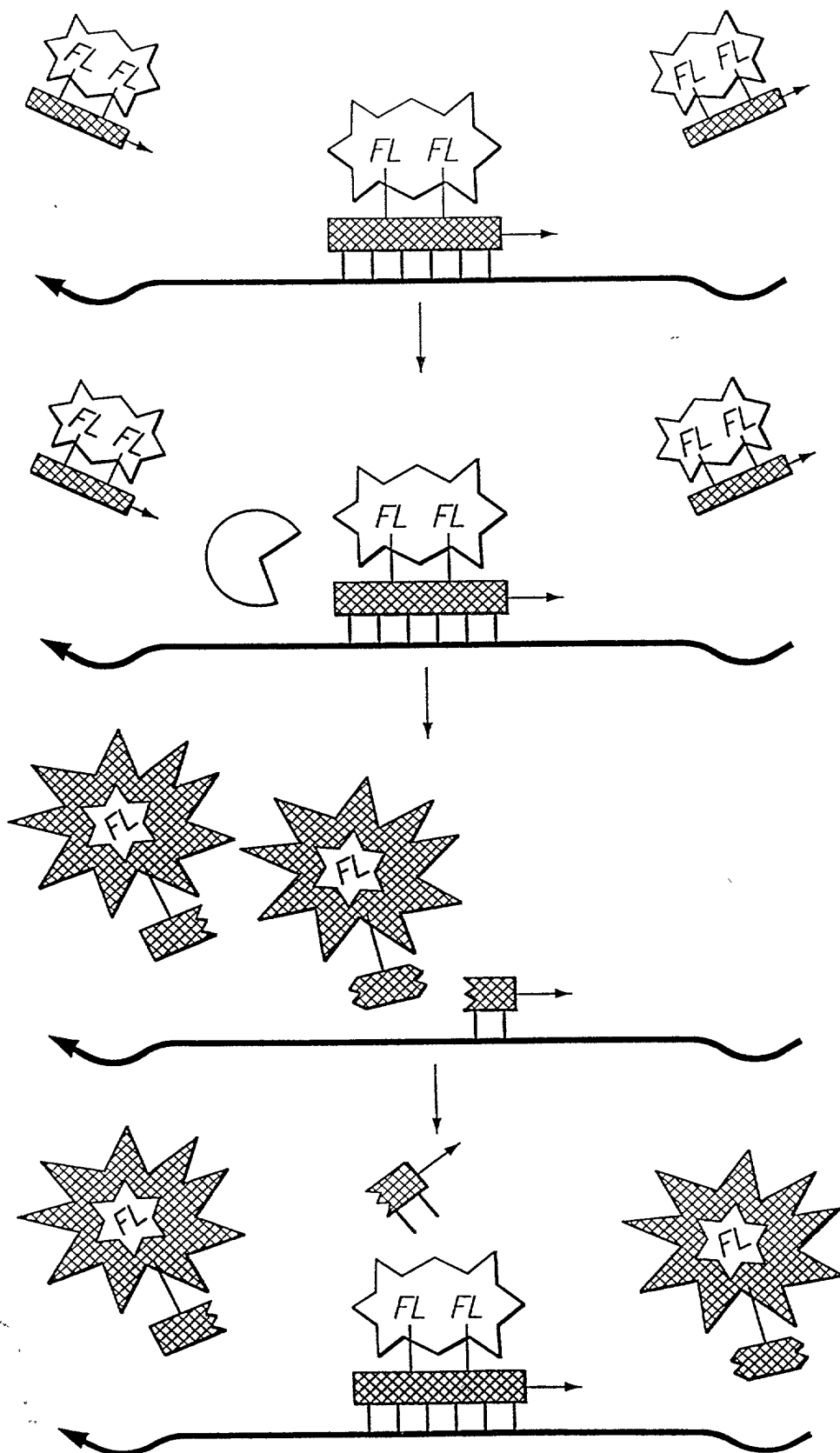


FIG. 27

10081305-060702

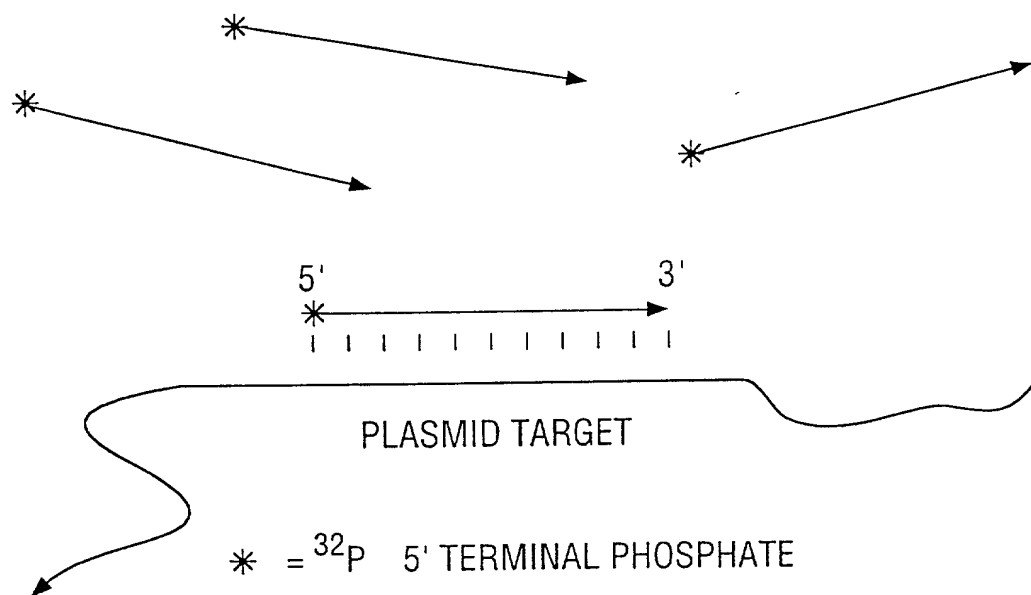


FIG. 28A

10081306.050702

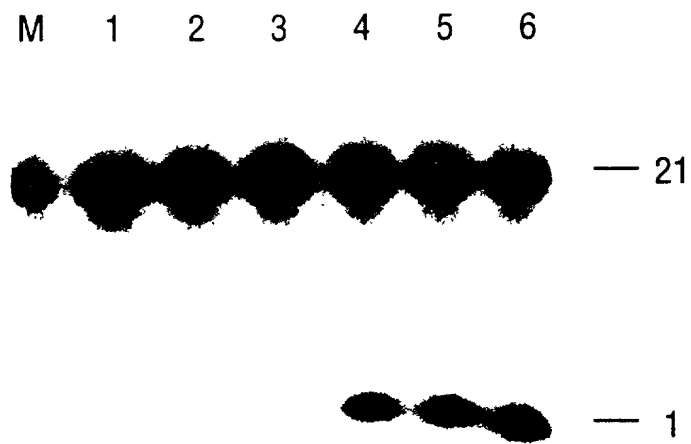
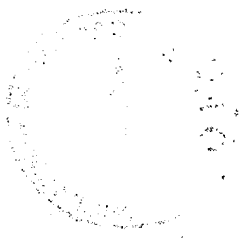
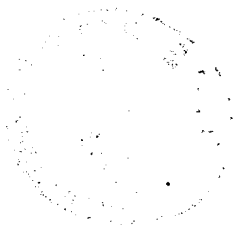


FIG. 28B





201090" 90815007

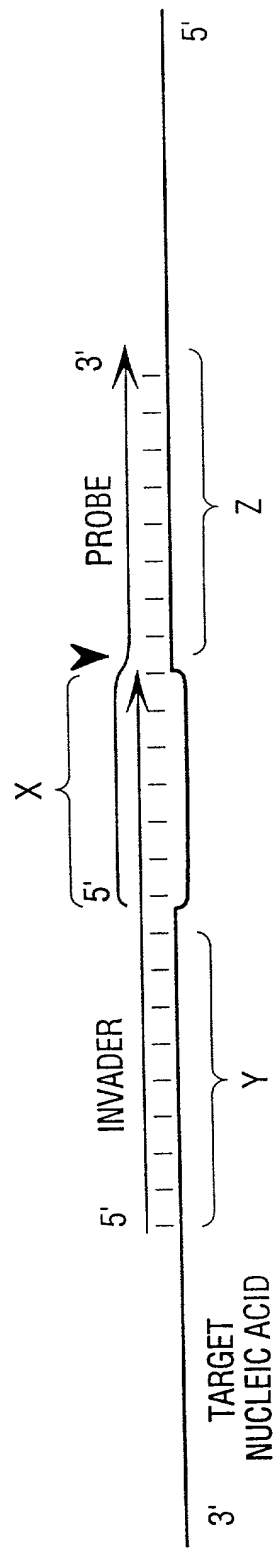


FIG. 29

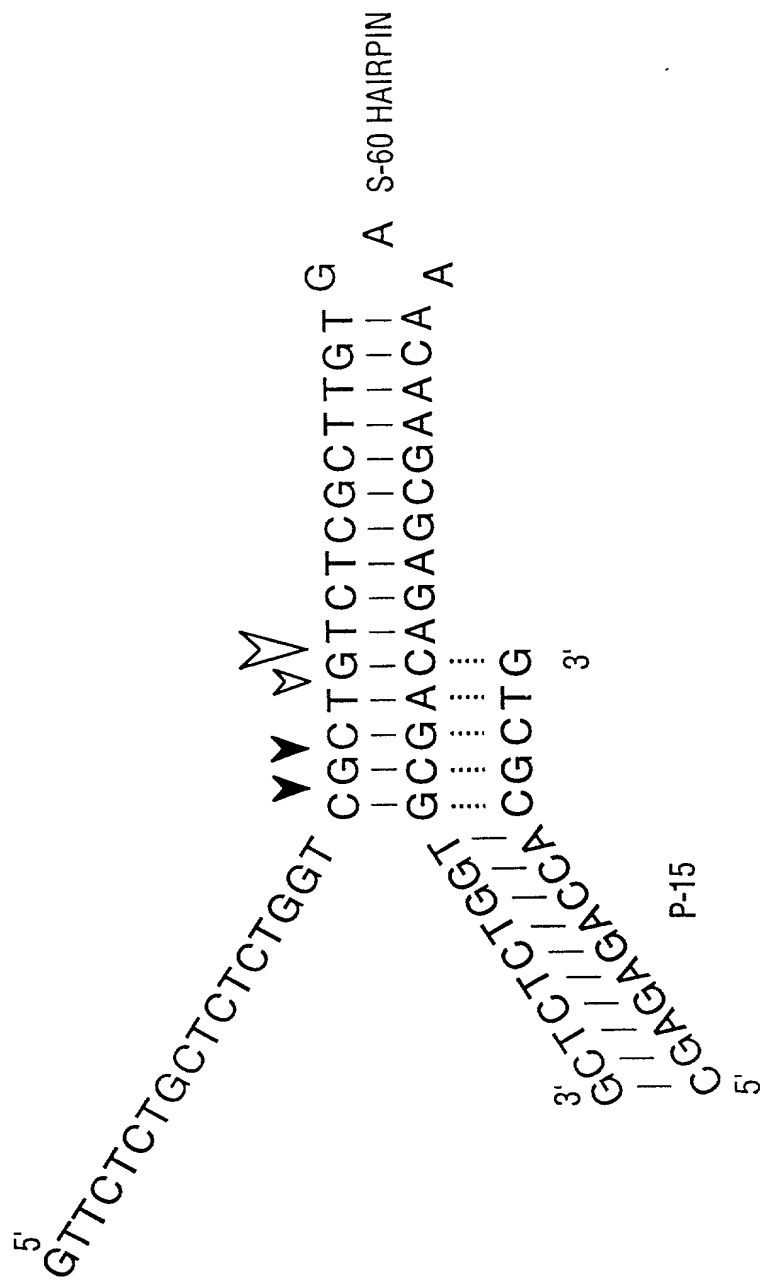


FIG. 30

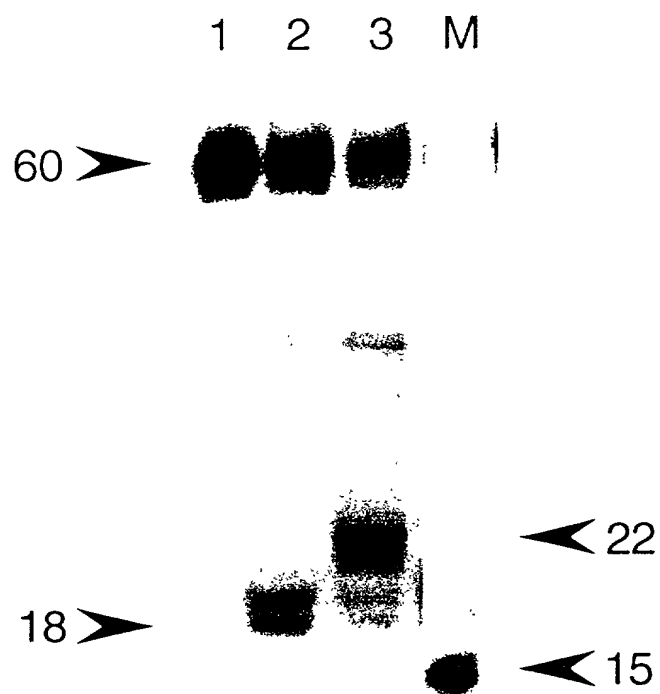


FIG. 31

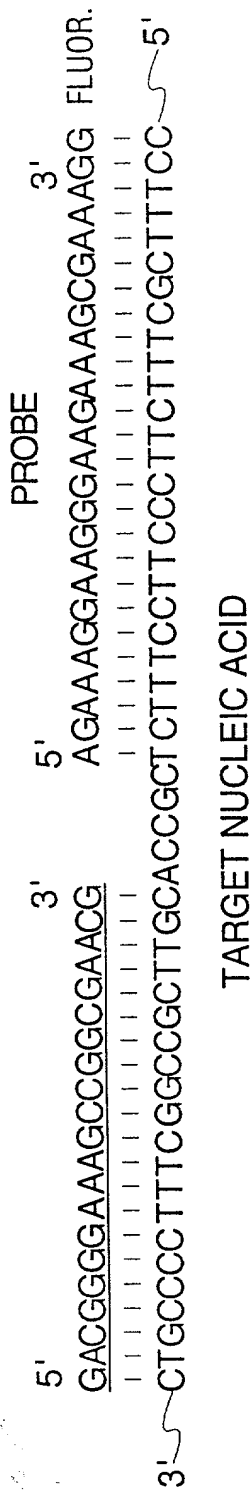


FIG. 32A

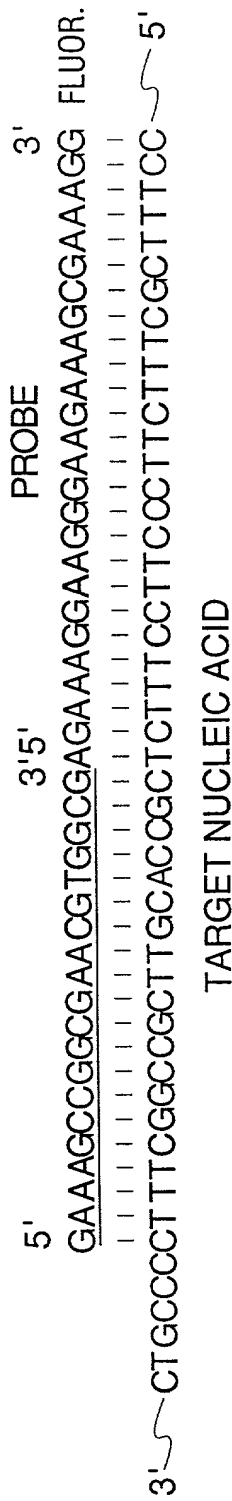


FIG. 32B

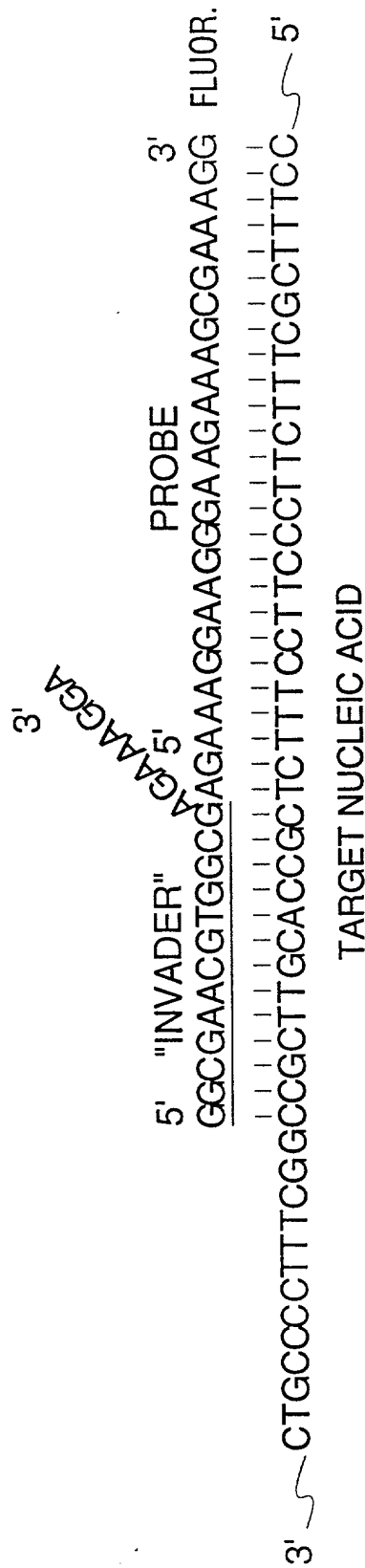


FIG. 32C

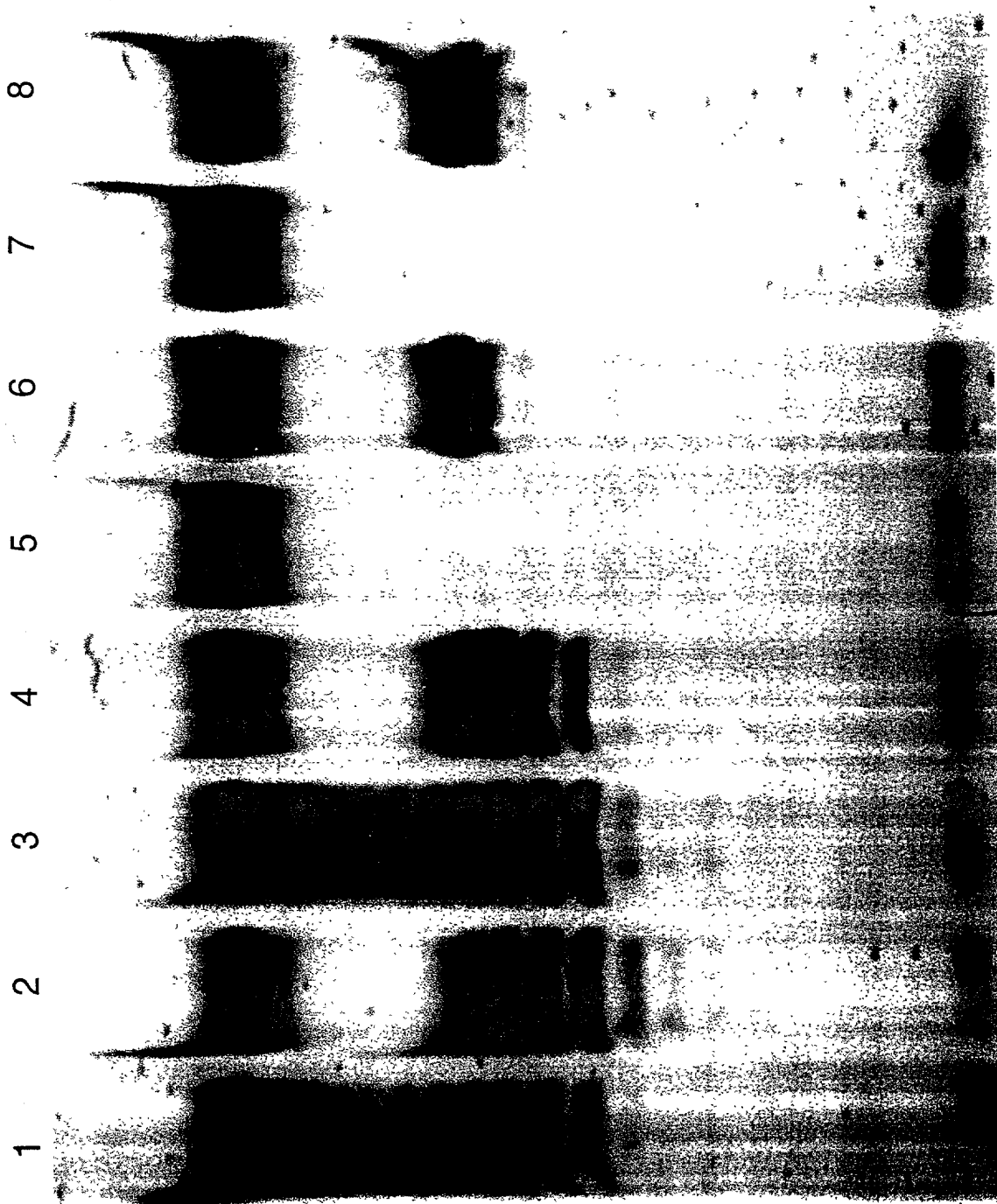


FIG. 33

201090" 90818001

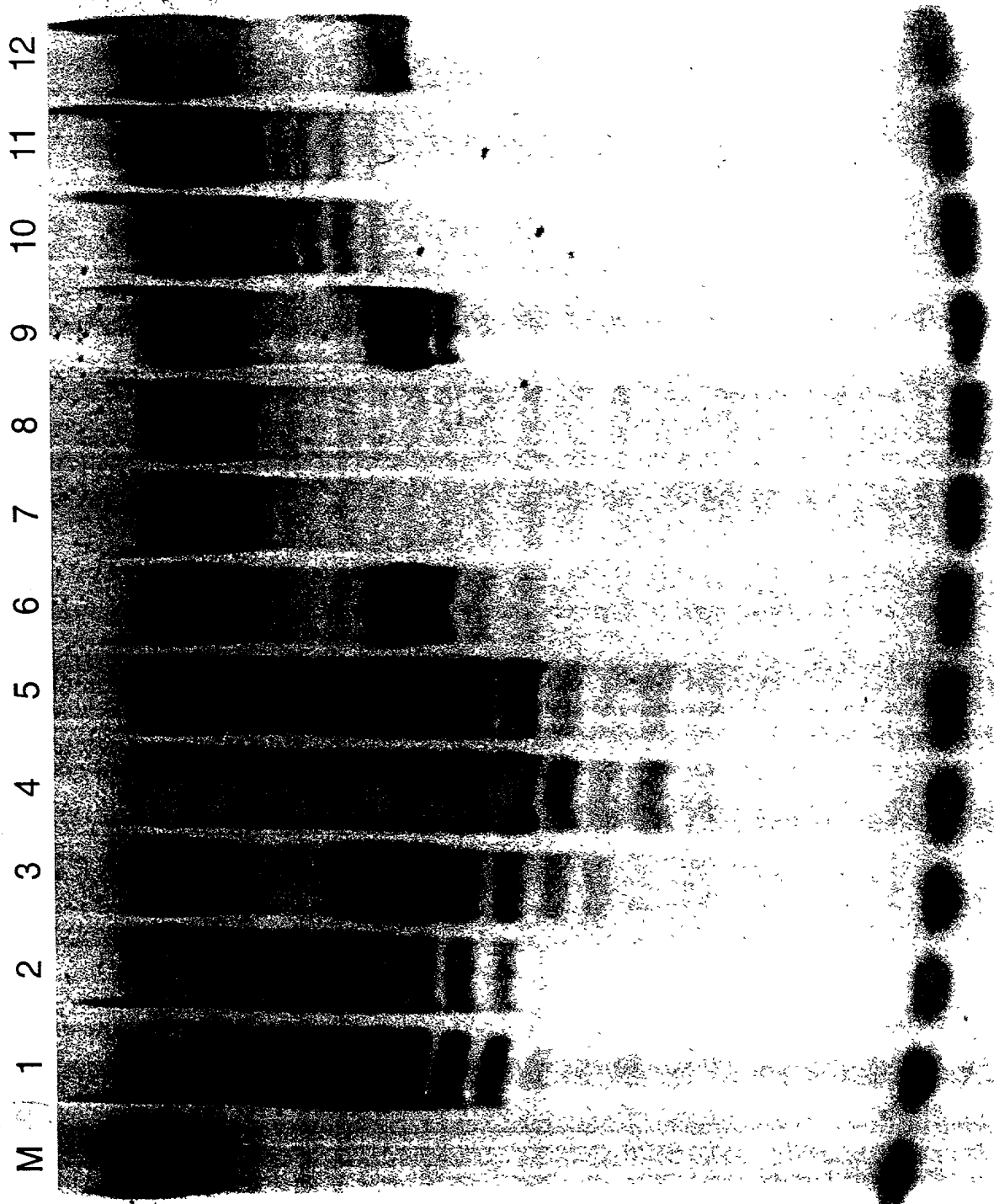


FIG. 34

10081806-050702

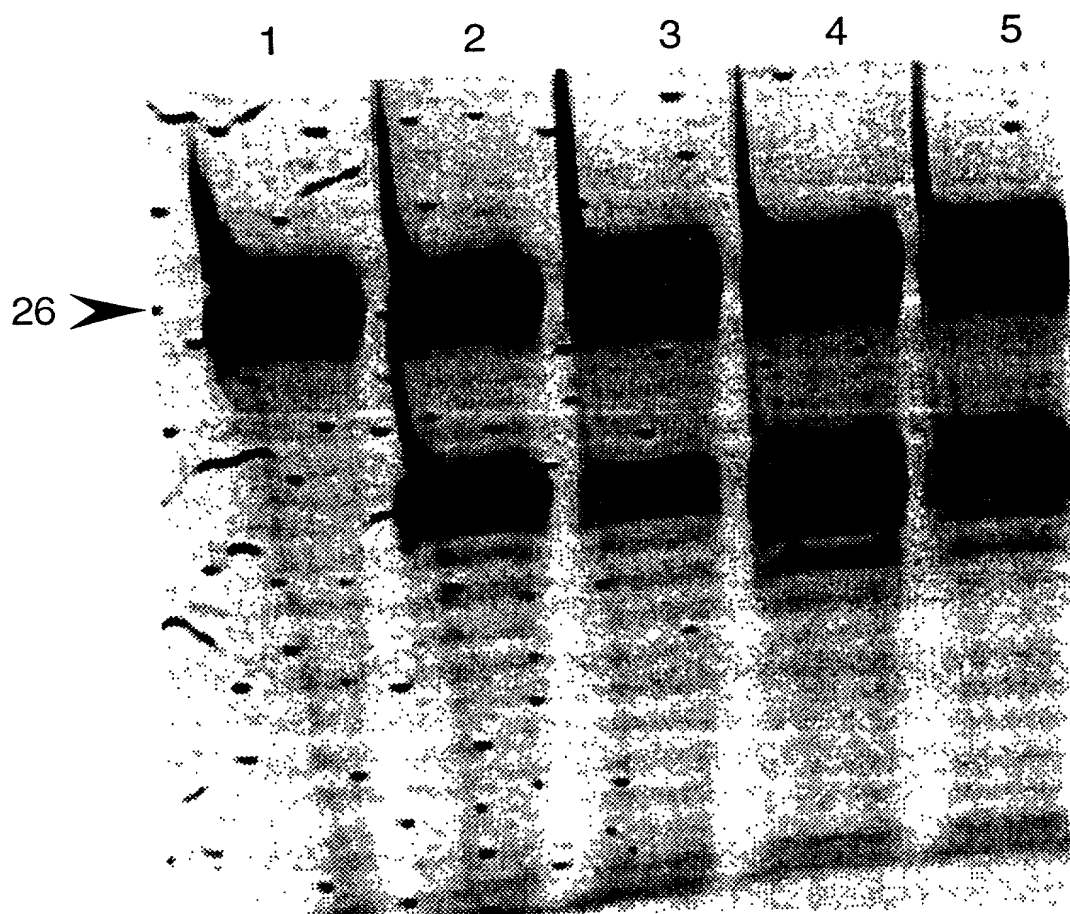


FIG. 35

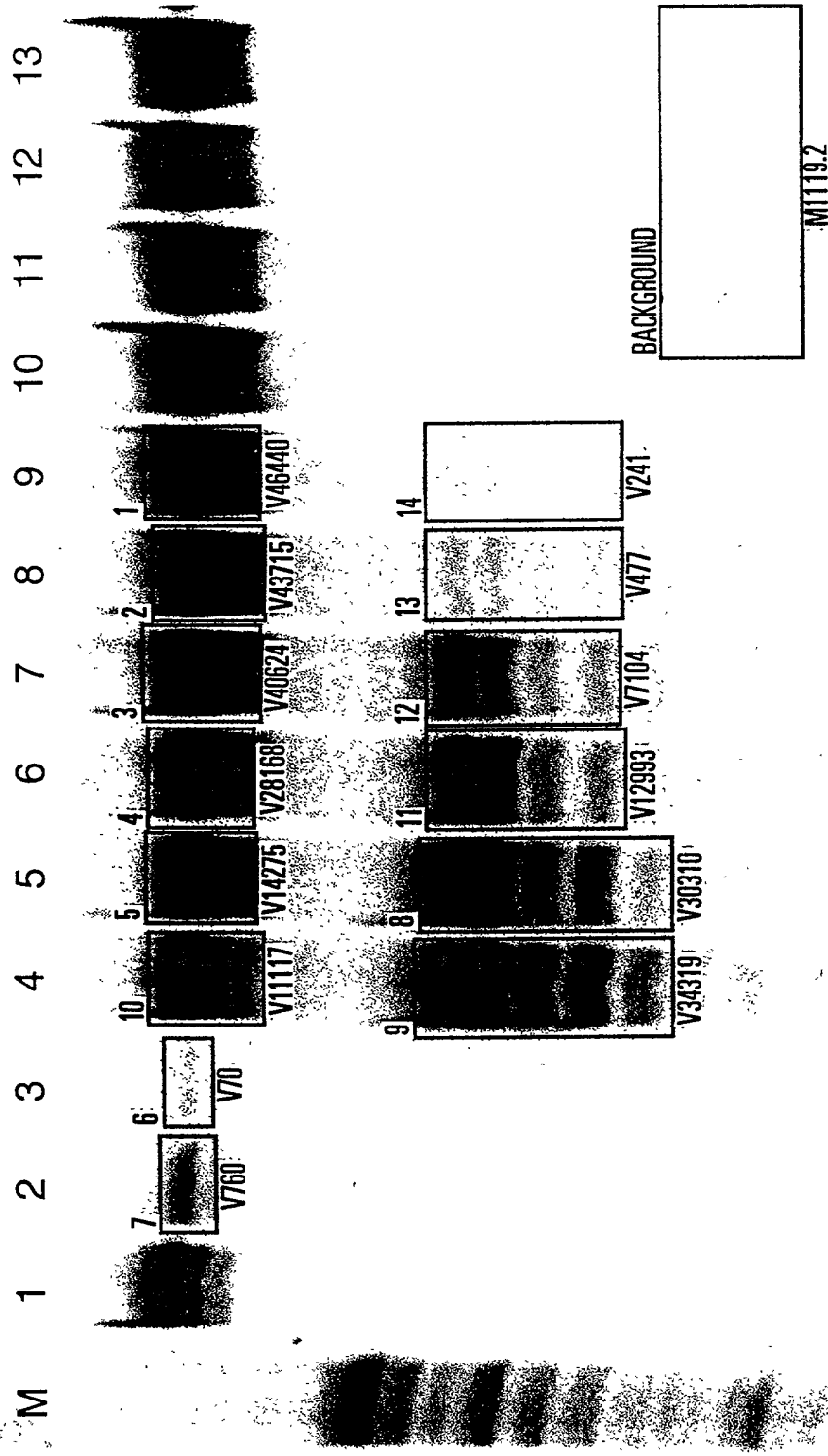


FIG. 36

204090-908T800T

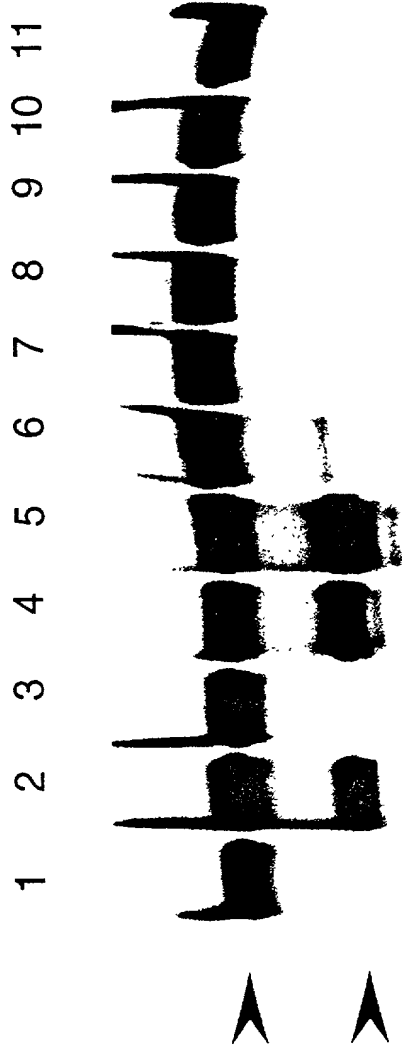


FIG. 37

204090-90818001

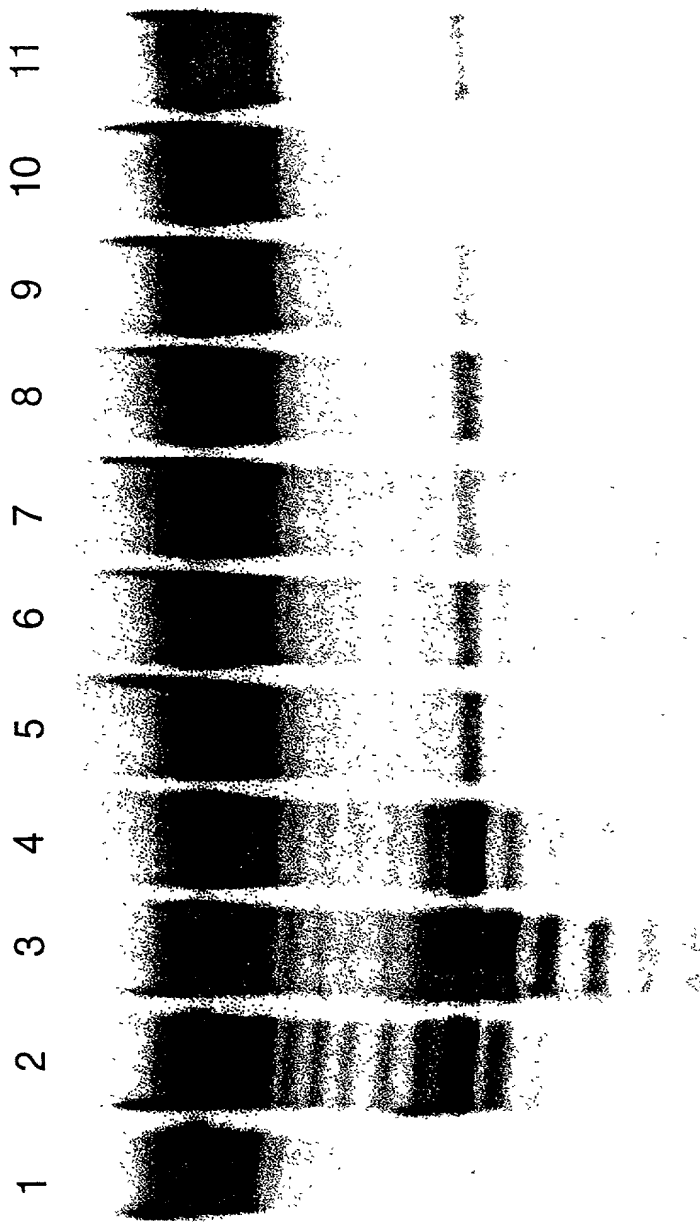


FIG. 38

10081805, 050302

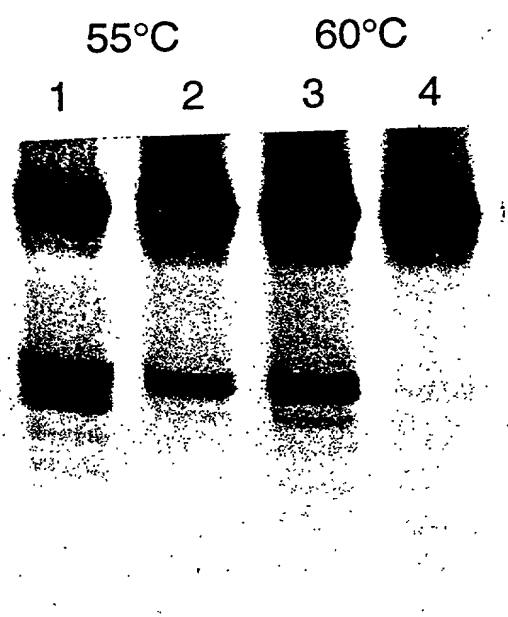


FIG. 39

20081906-060702

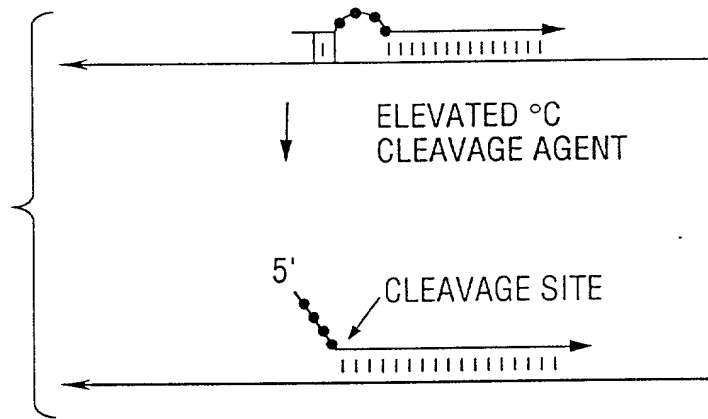


FIG. 40A

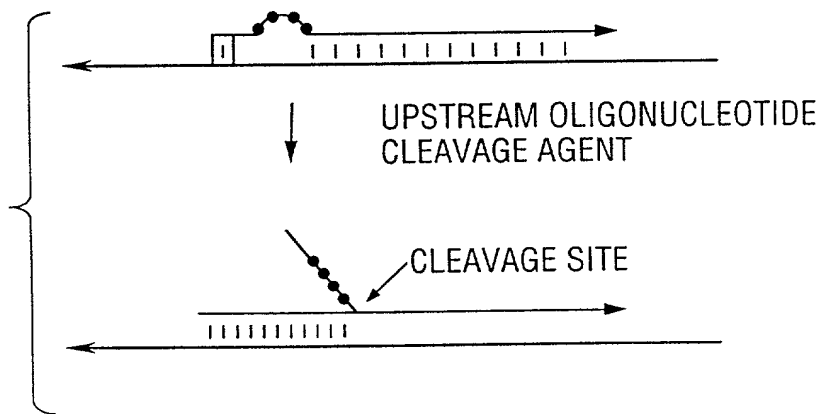


FIG. 40B

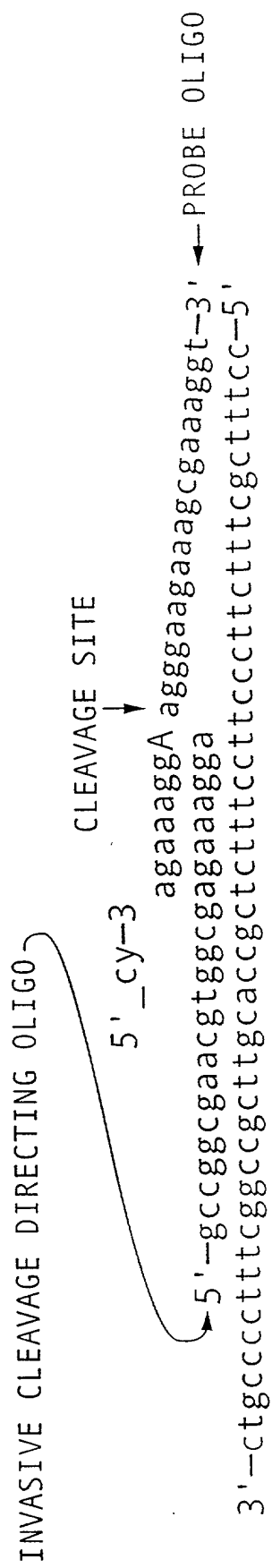


FIG. 41

10081805.060702

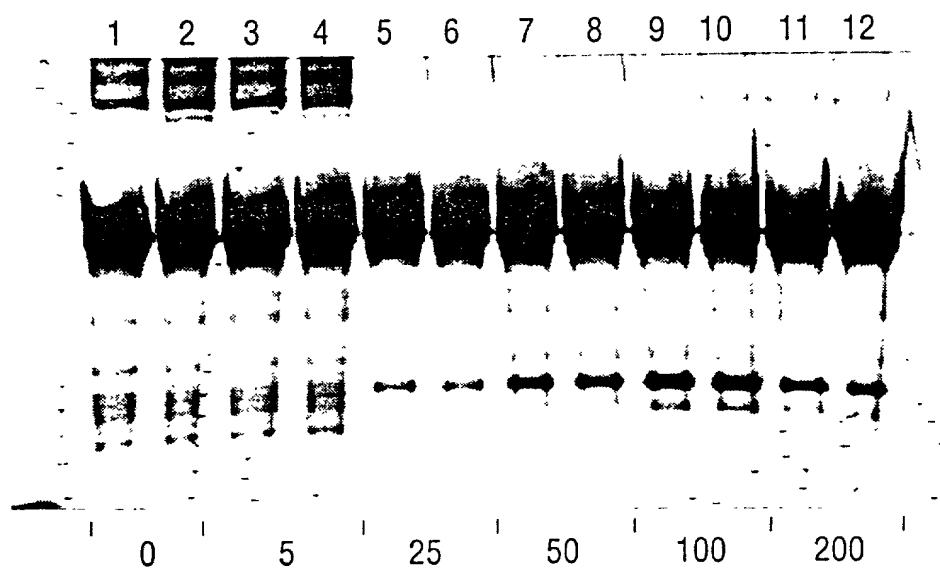


FIG. 42

1 2 3 4 5 6 7 8 9 10

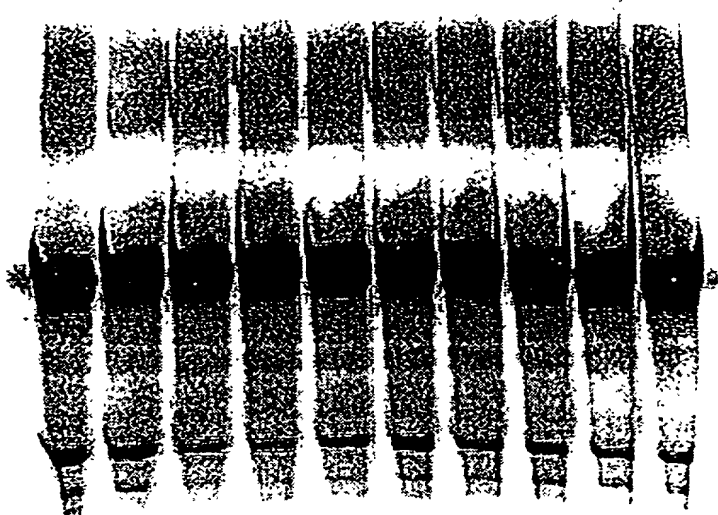


FIG. 43

10081806.050702

1 2 3 4 5 6 7 8 9 10 11 12 13 14

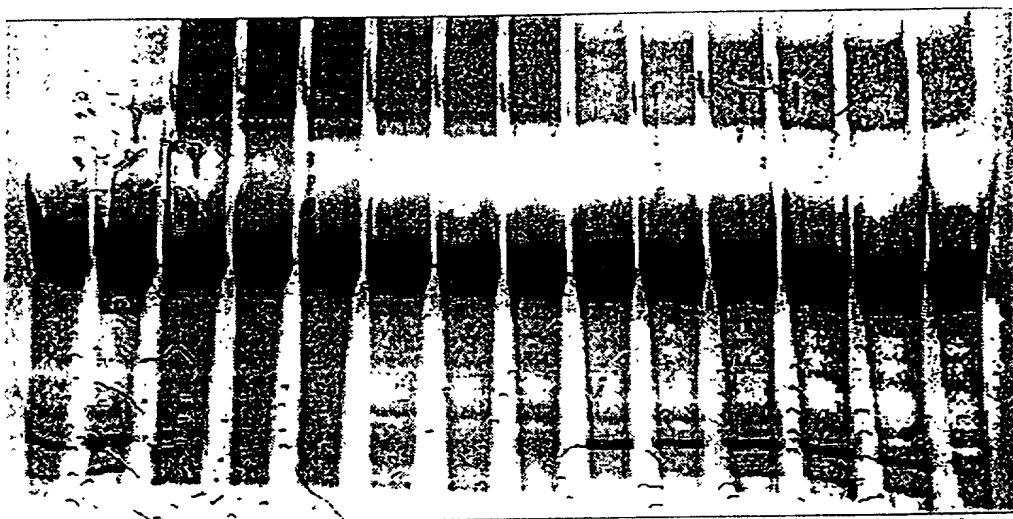


FIG. 44

10081806.060702

202090* 50878007

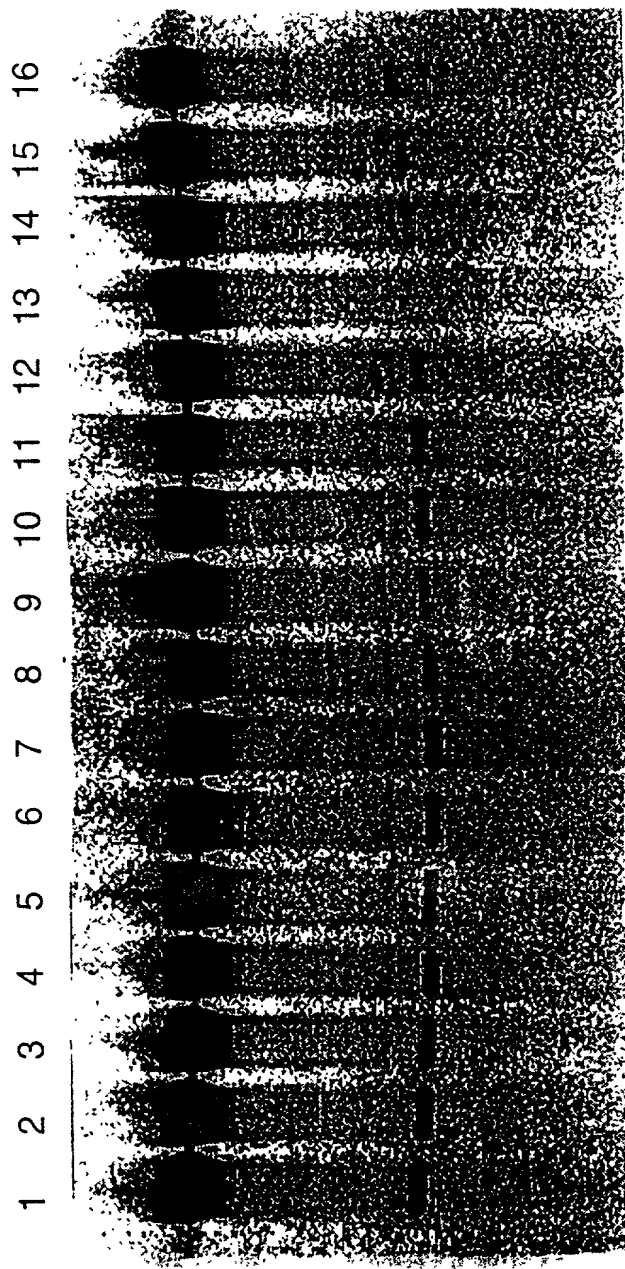


FIG. 45

10081806.060702

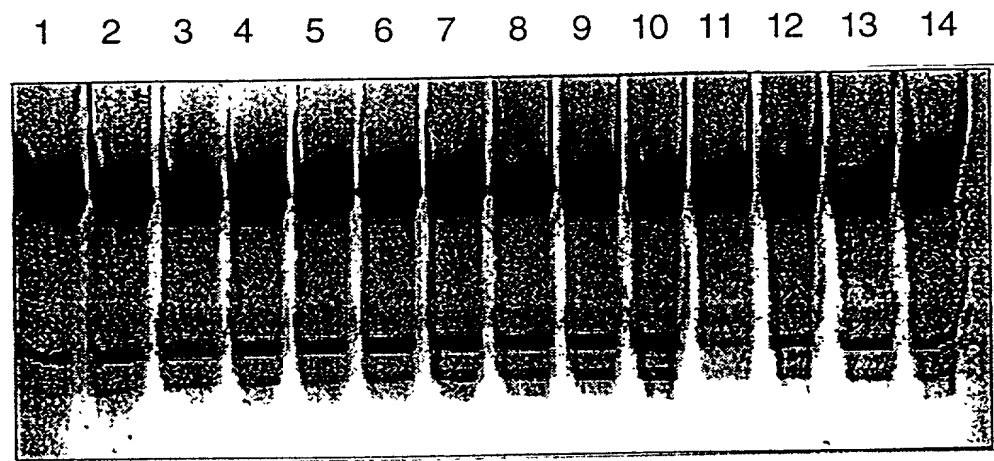


FIG. 46

204090-9087800T

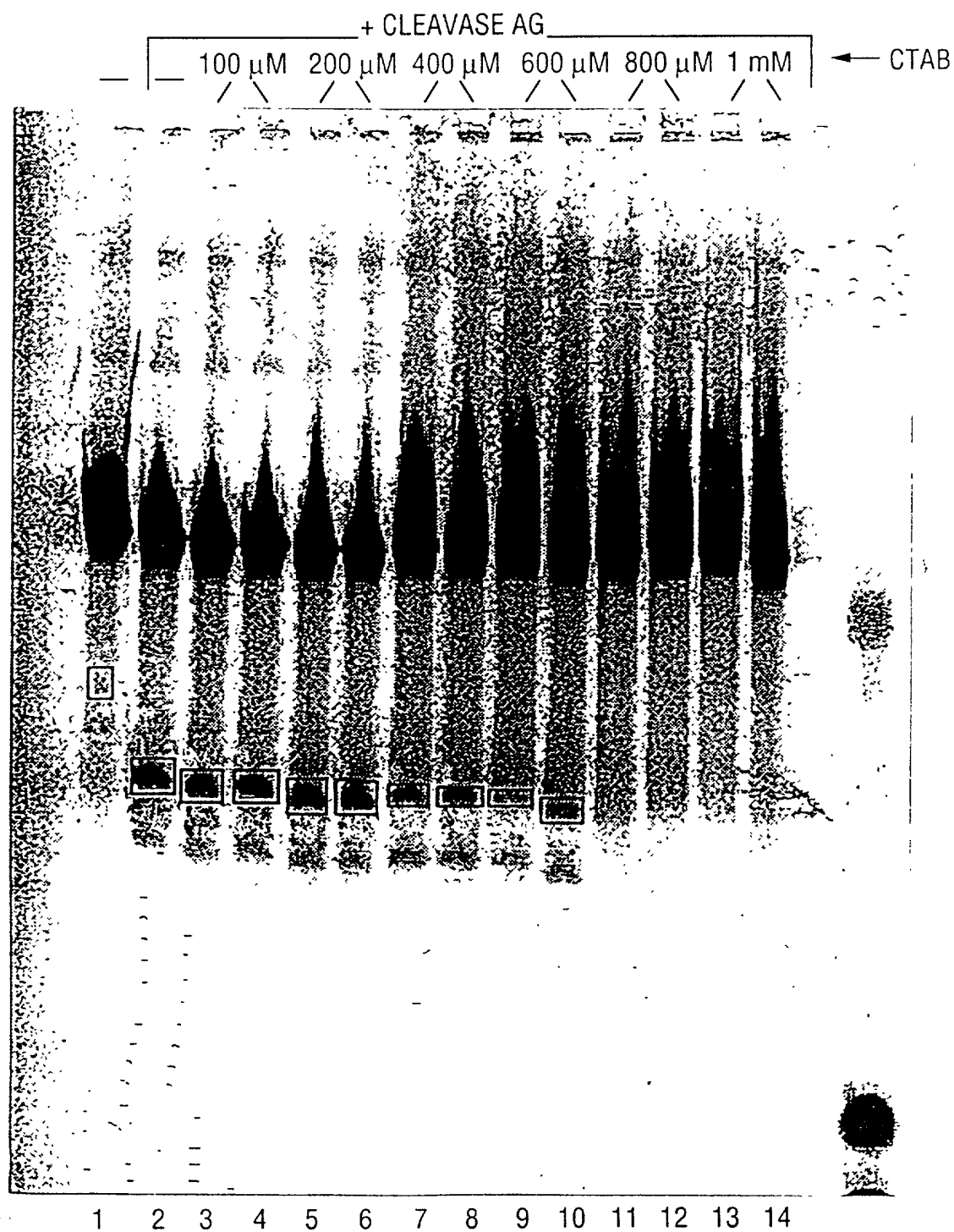


FIG. 47

10081805.050702

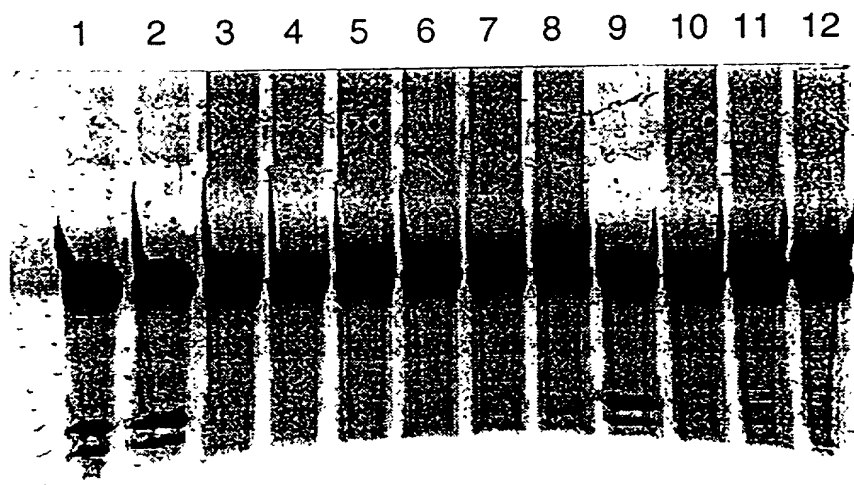


FIG. 48

10081306, 060702

1 2 3 4 5 6 7 8

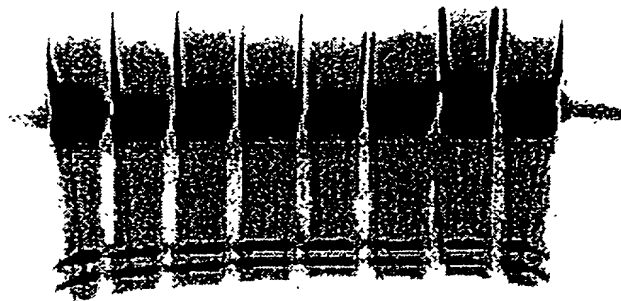


FIG. 49

10081905_050702

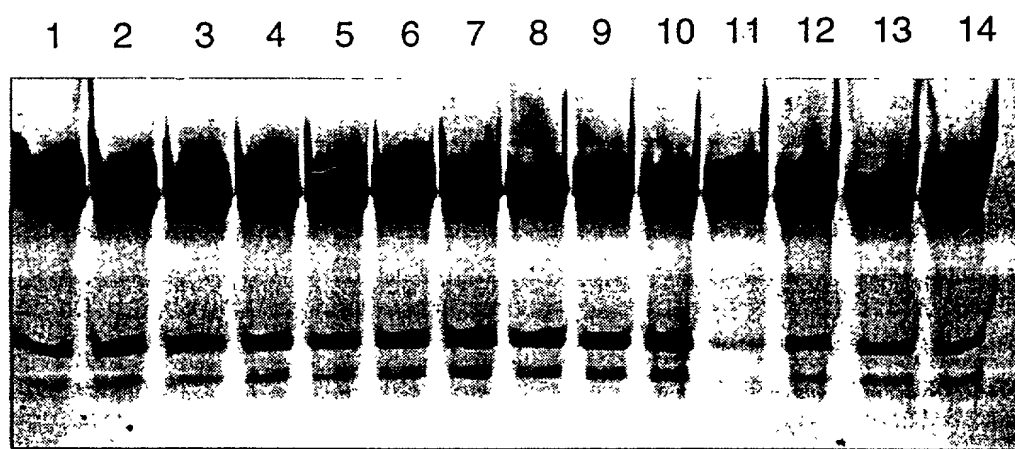


FIG. 50

10081805-050702

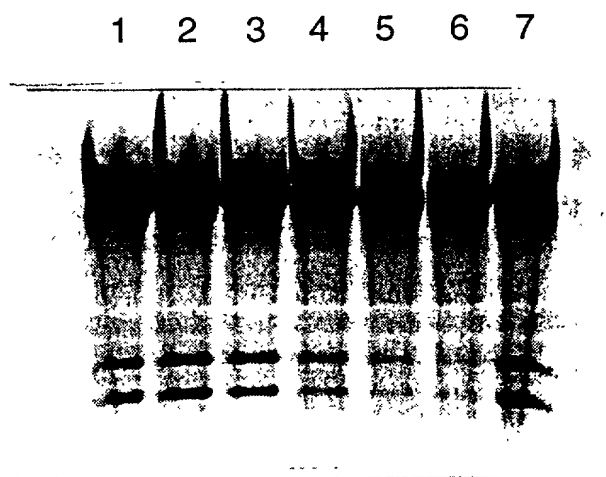


FIG. 51

10081806 .050302

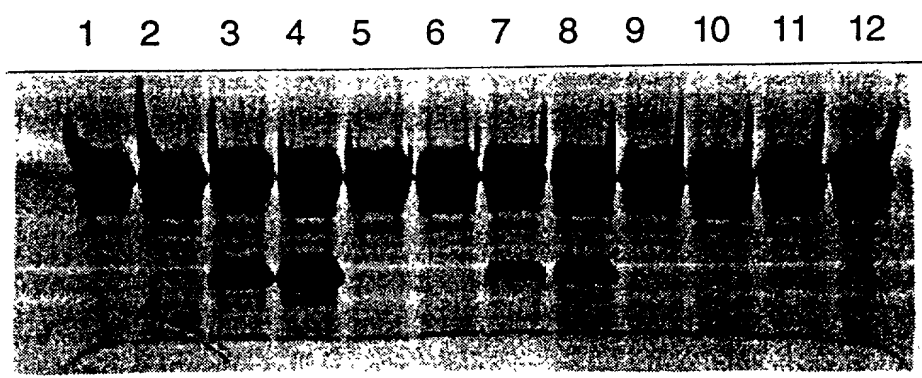


FIG. 52

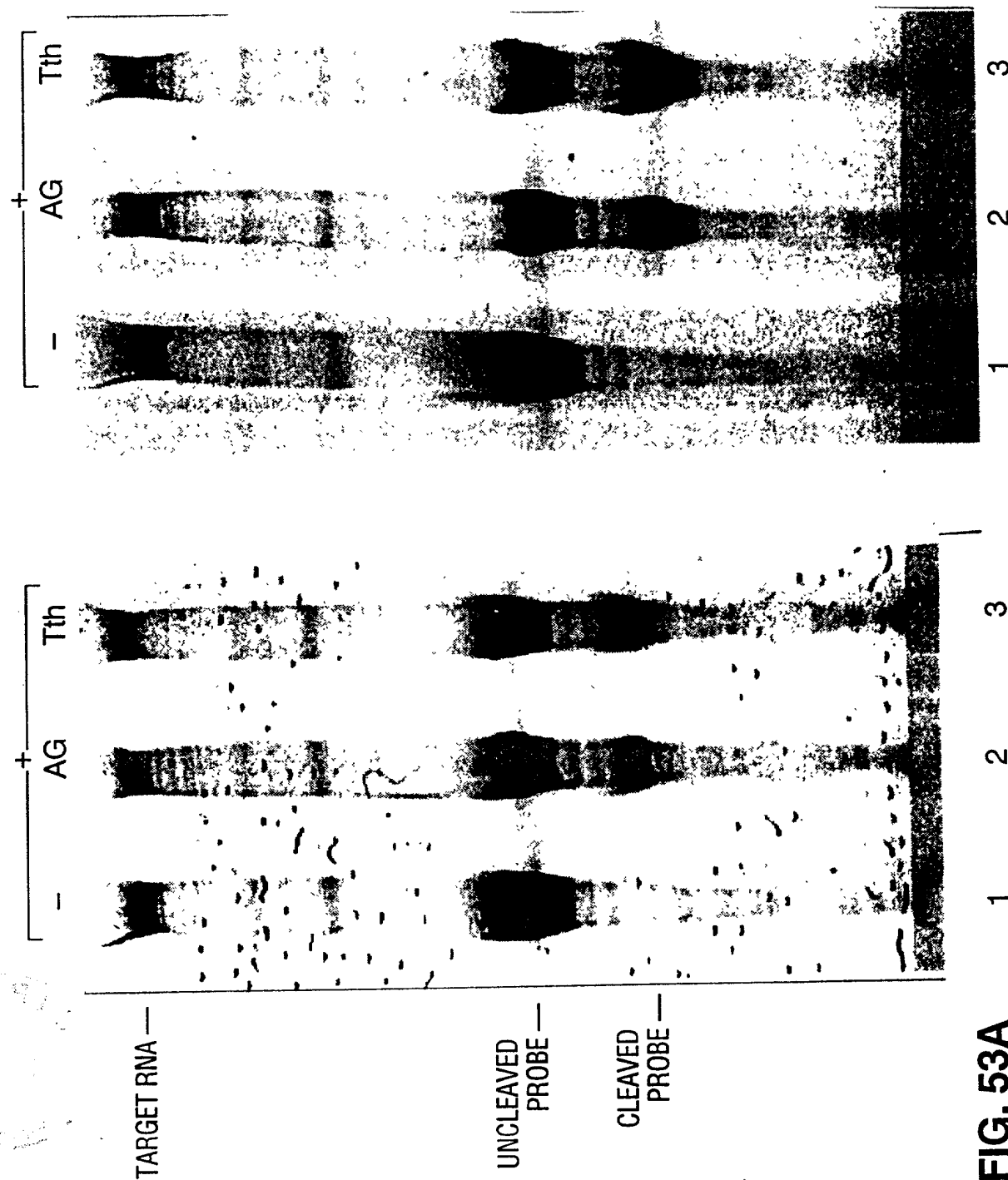


FIG. 53B

204090" 908T800T

— ENZYME
— TARGET (fmol)
— RNA

500 1 5 10 50 100 100 1 5 10 50 100

CLEAVASE AG Tth

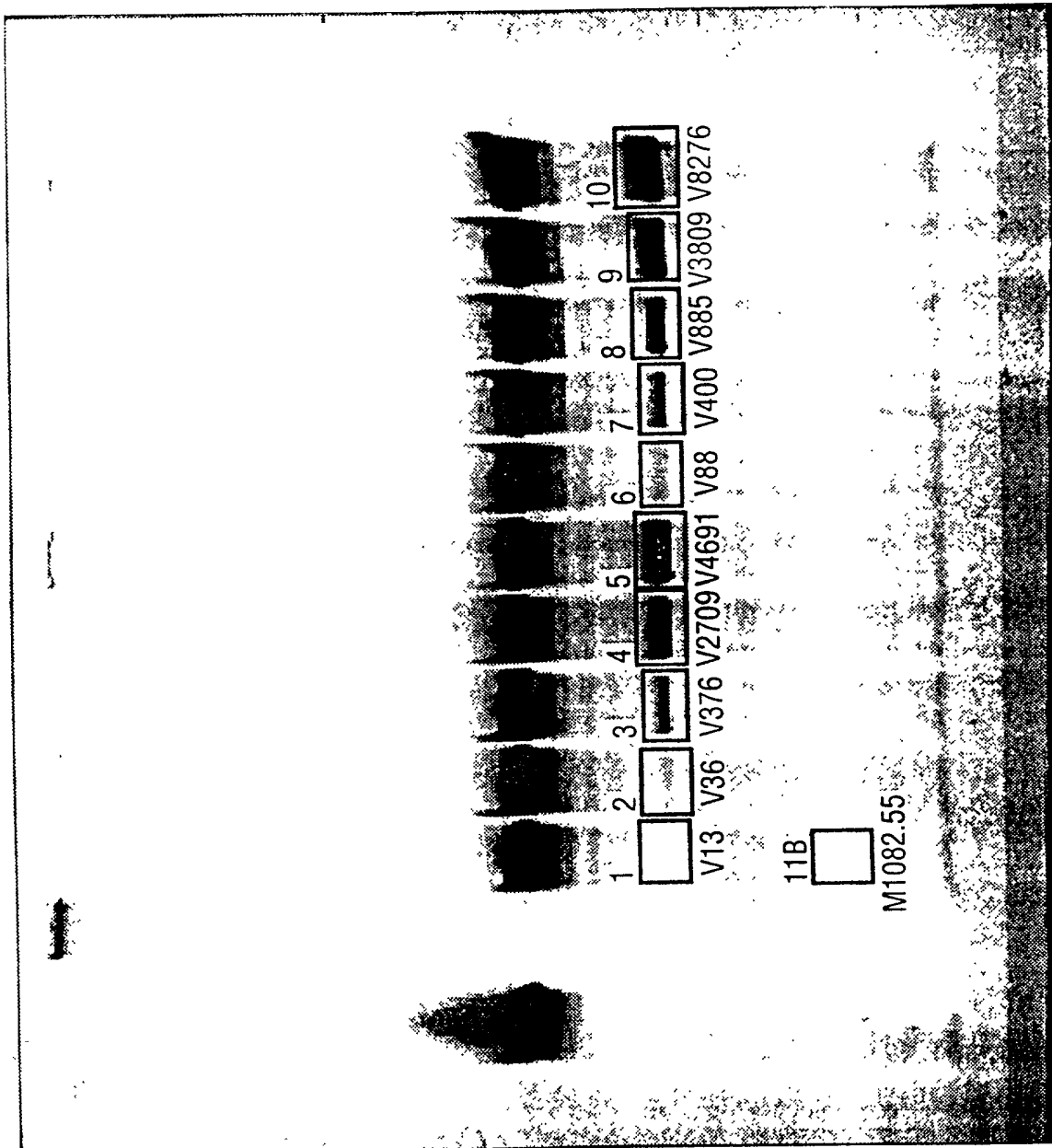


FIG. 54

10081806, 060702

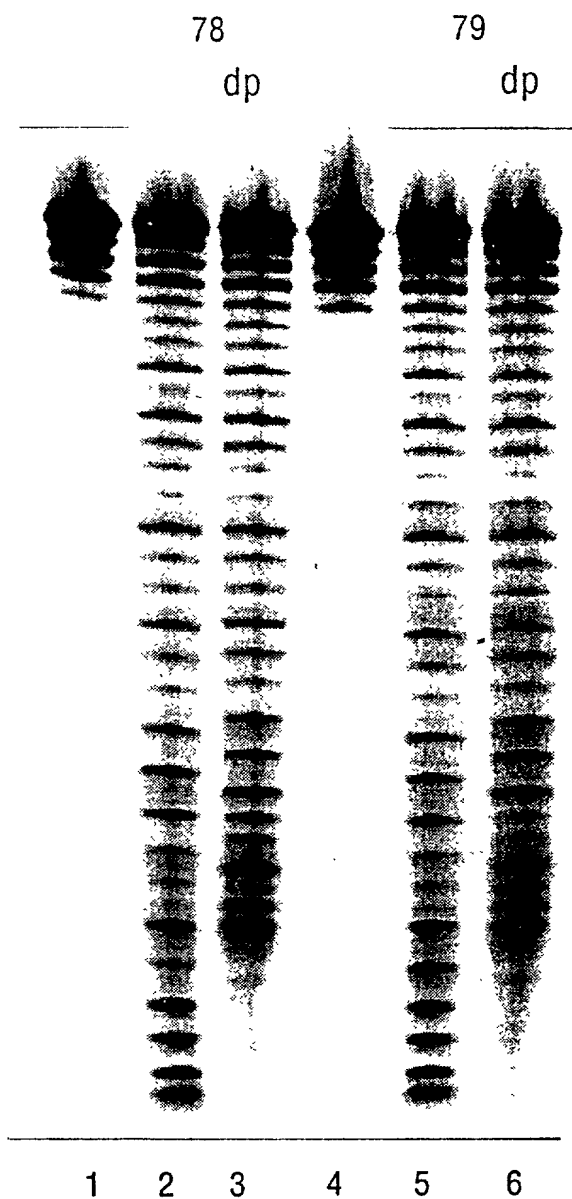


FIG. 55

70 (C10 amino T's)
74 (C6 amino T's)

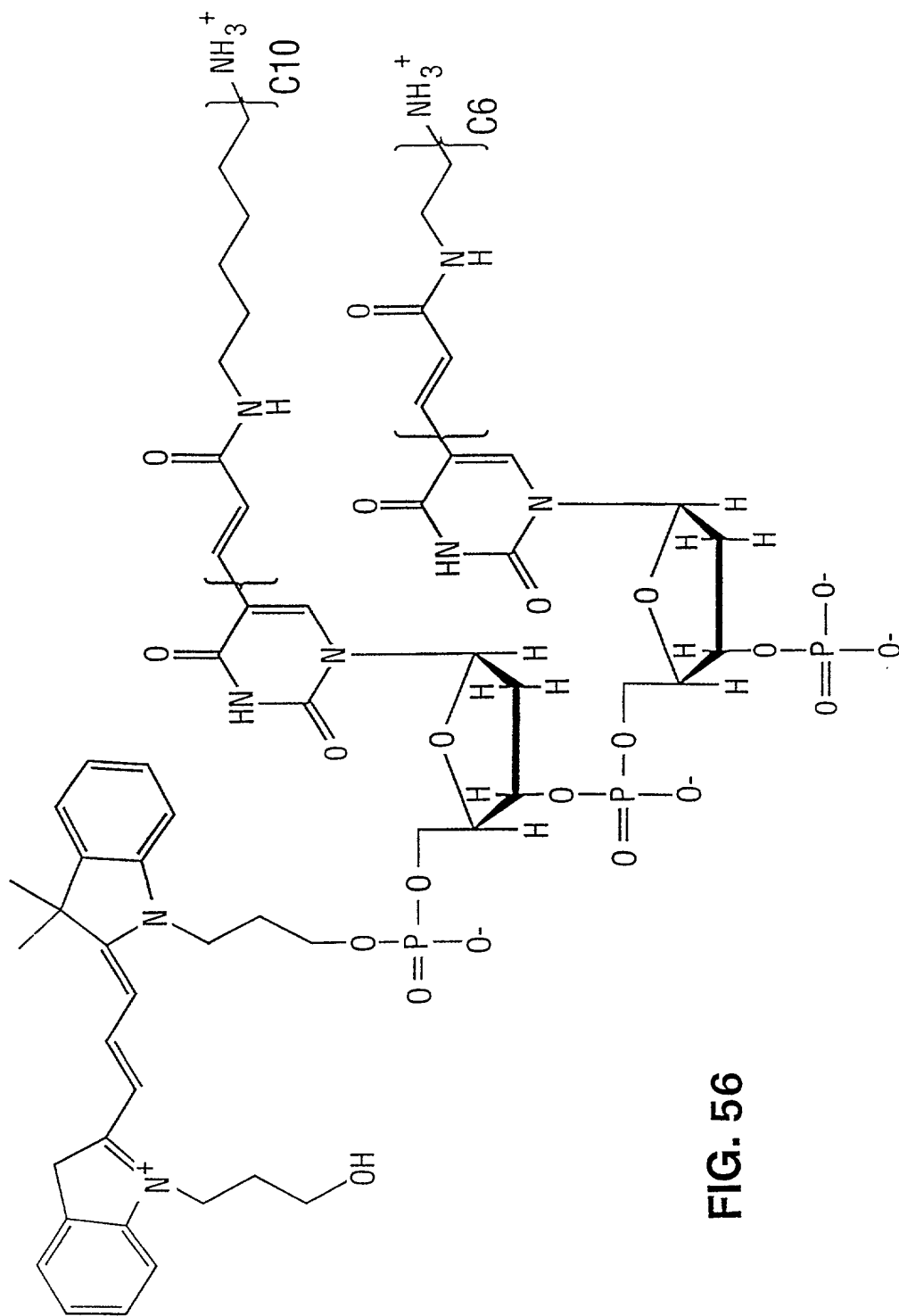


FIG. 56

75

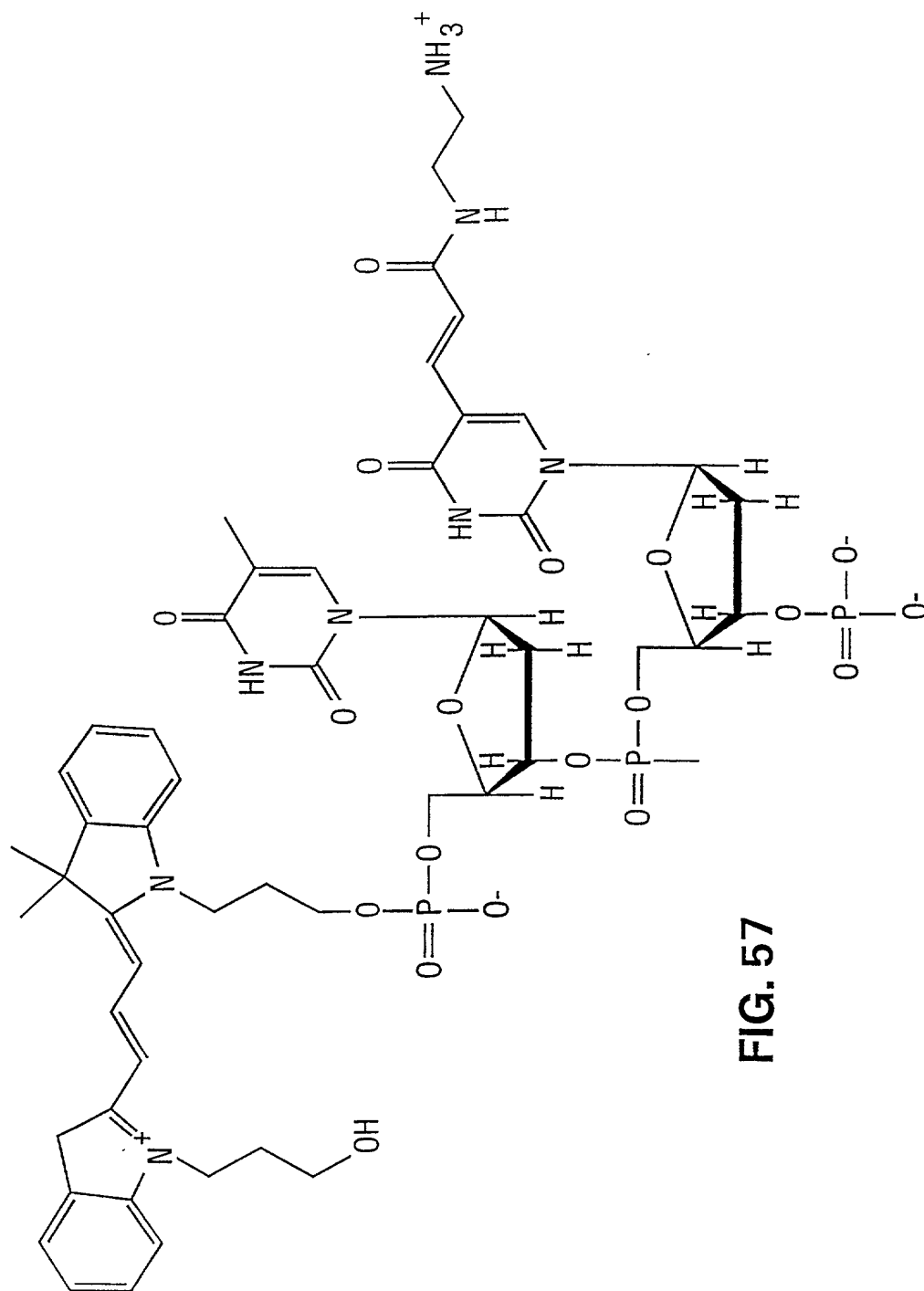


FIG. 57

76

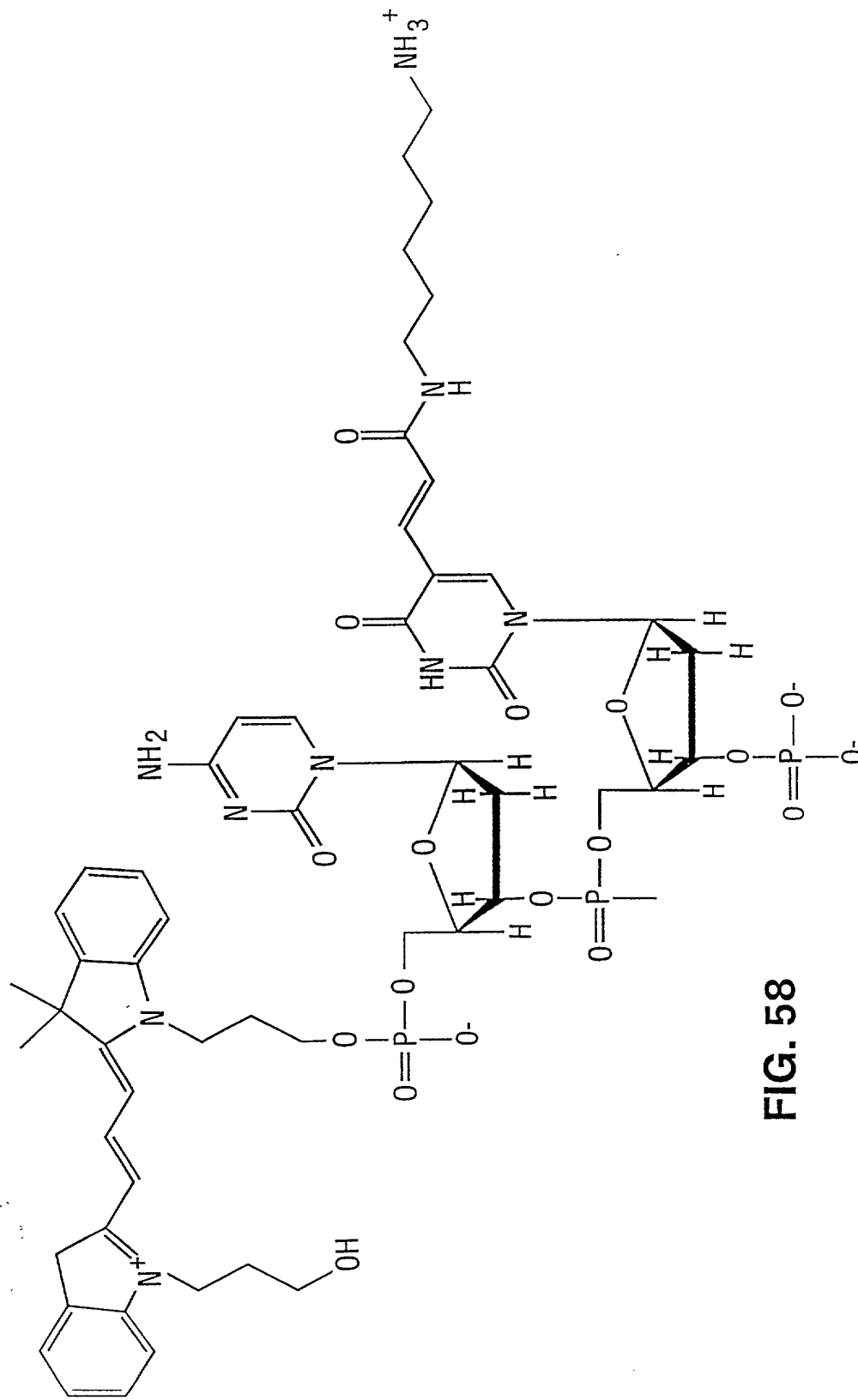


FIG. 58

10034805.050703

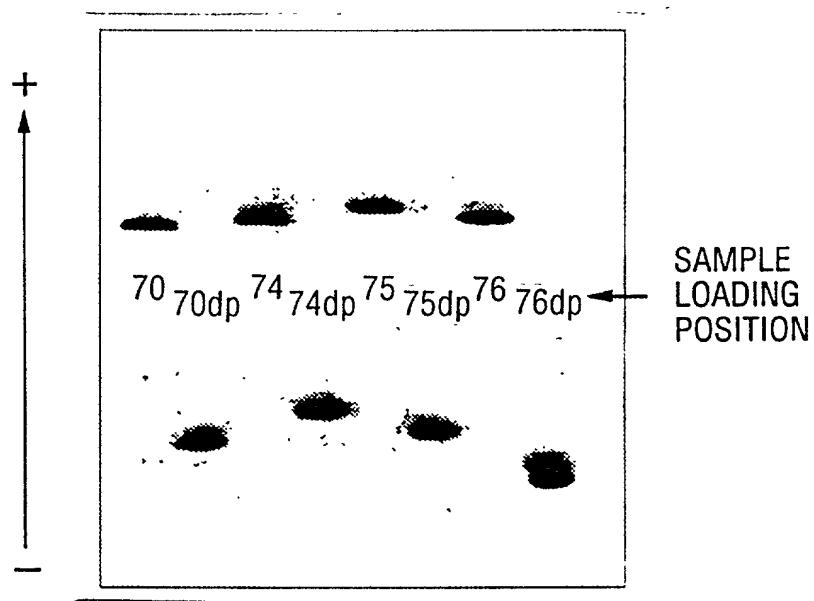


FIG. 59

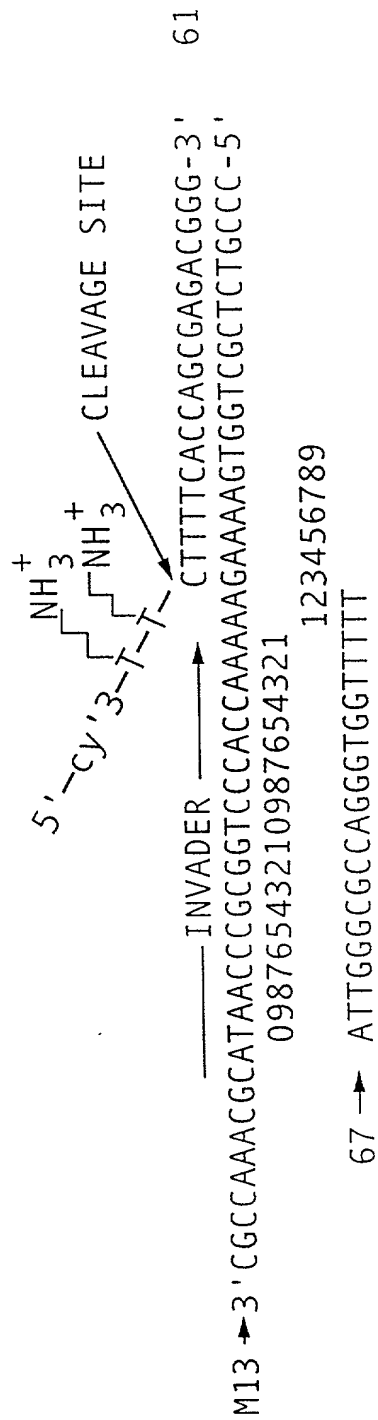


FIG. 60A

10091806.060702

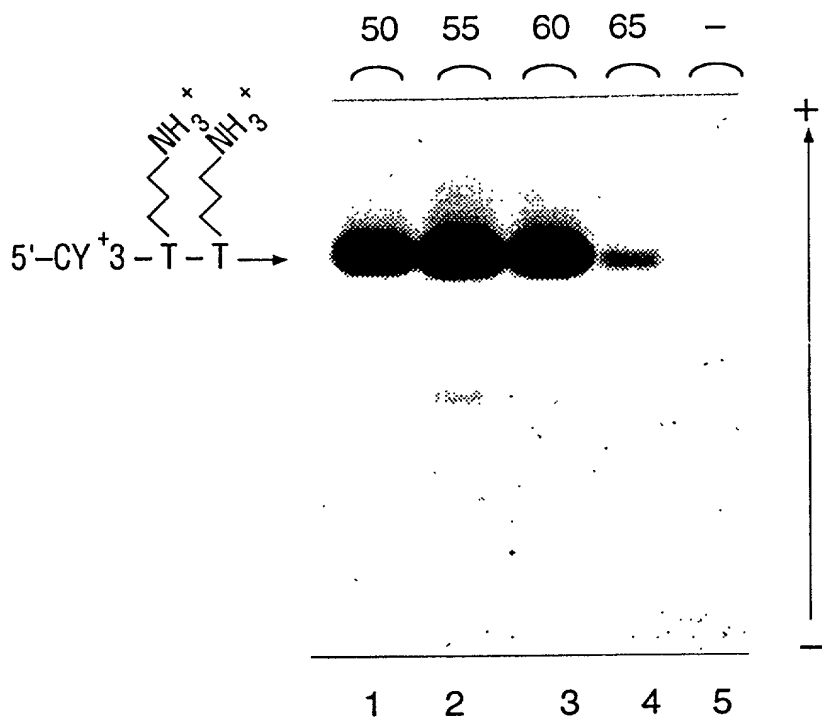


FIG. 60B

10081806.060702

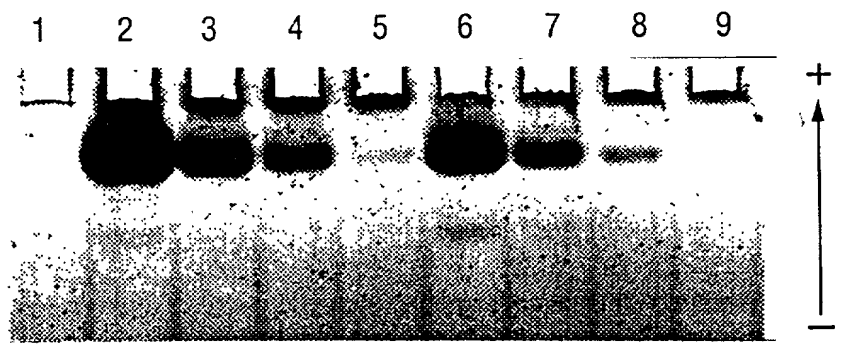
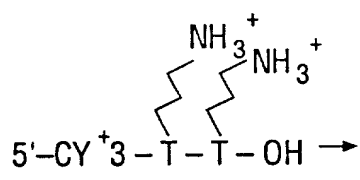


FIG. 61

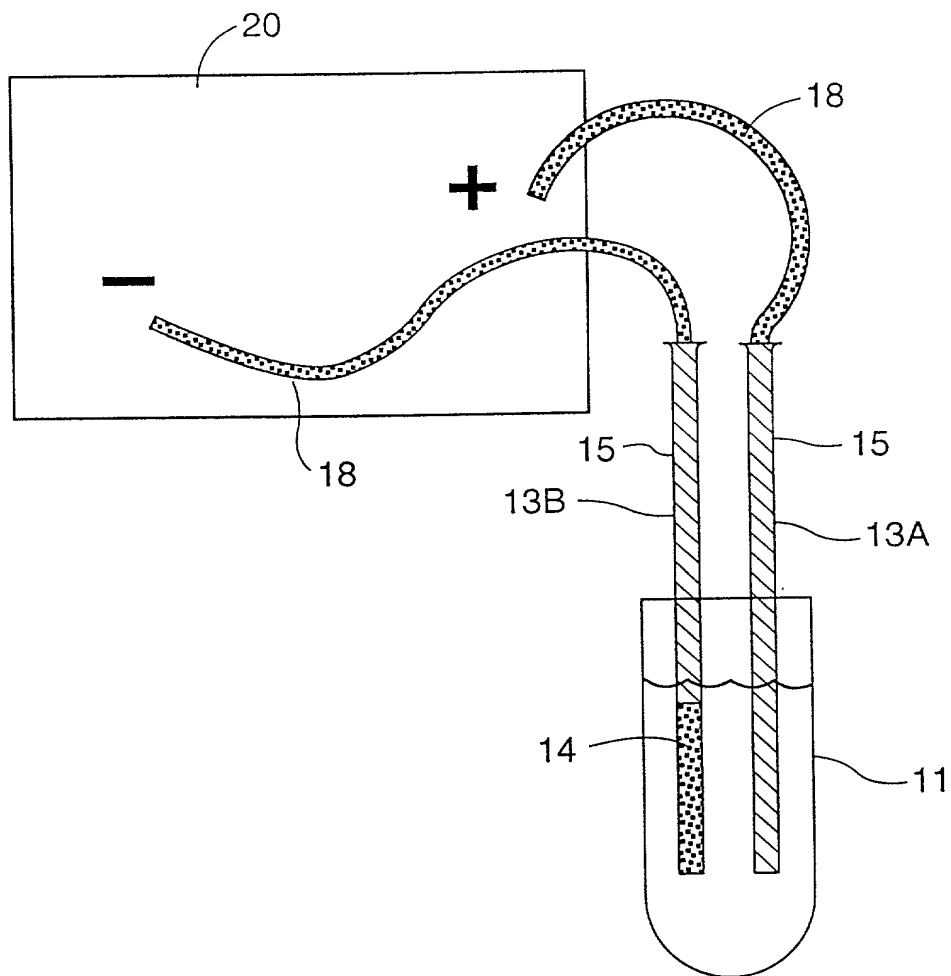


FIG. 62

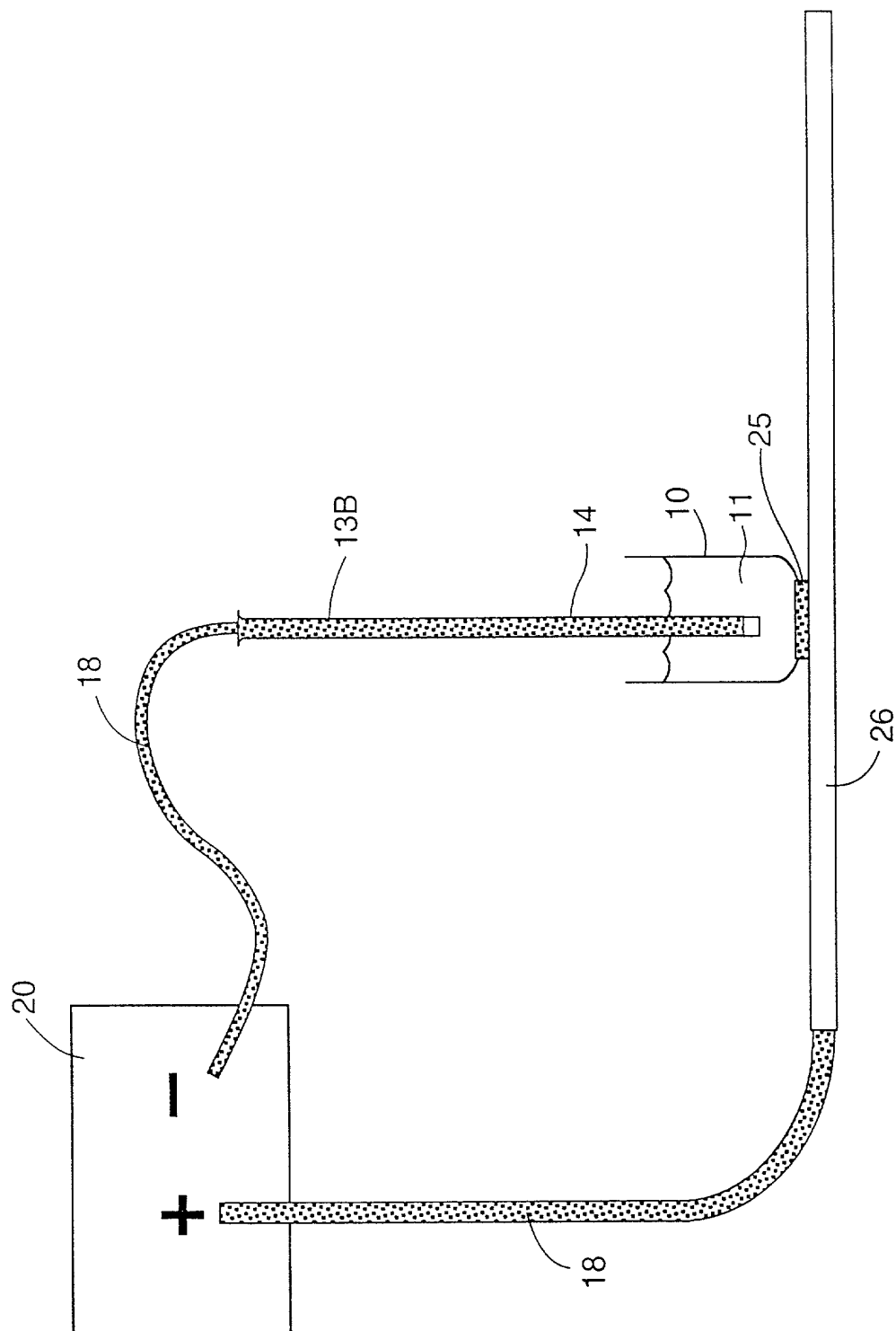


FIG. 63

10081805.060702

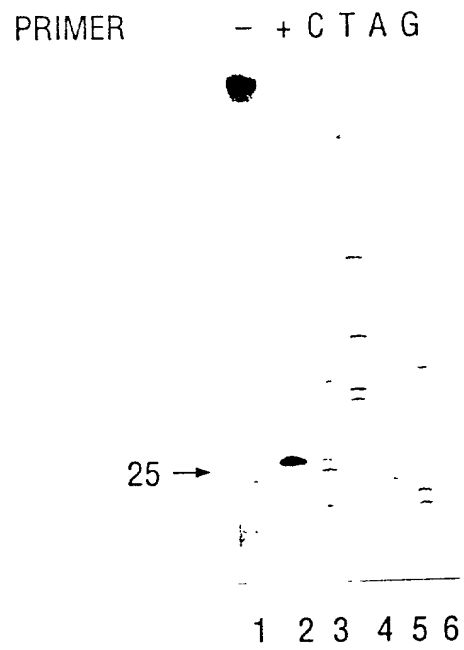


FIG. 64



FIG. 65A



FIG. 65B

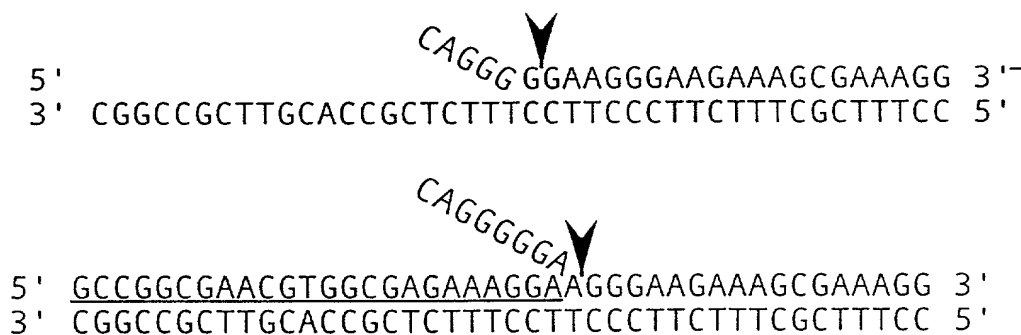


FIG. 65C



FIG. 65D

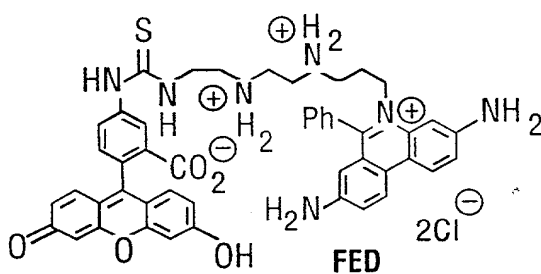
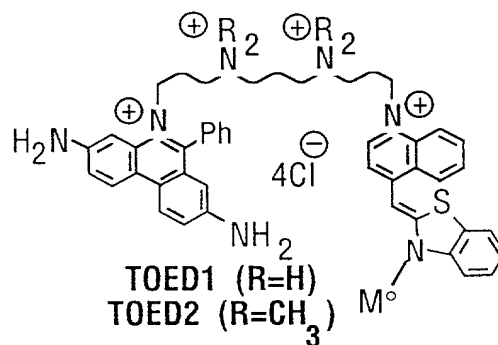
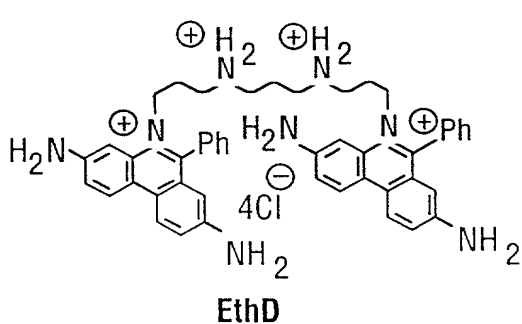
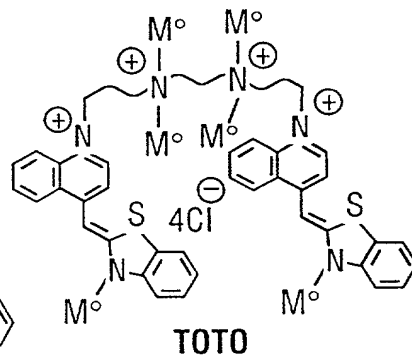
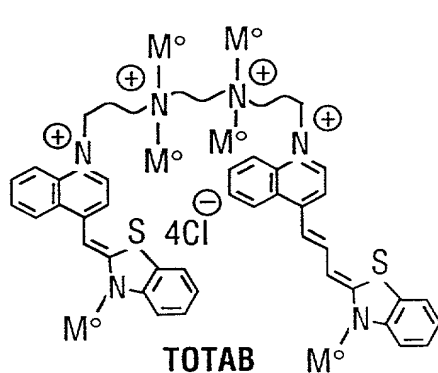
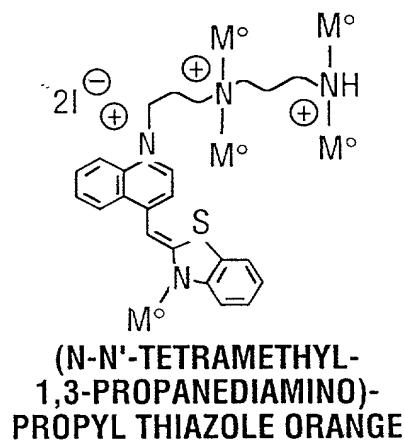
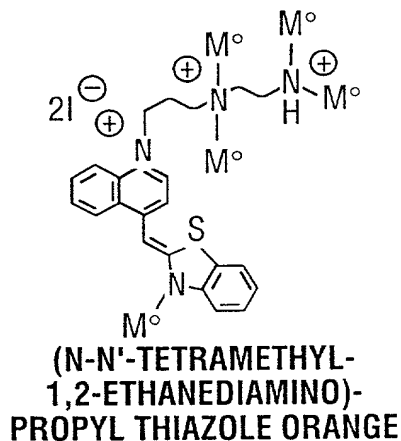
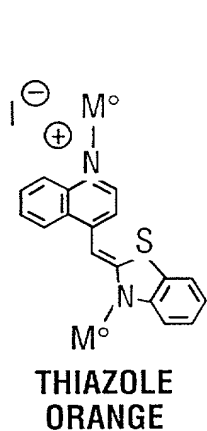
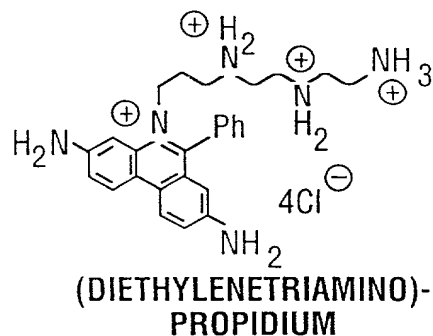
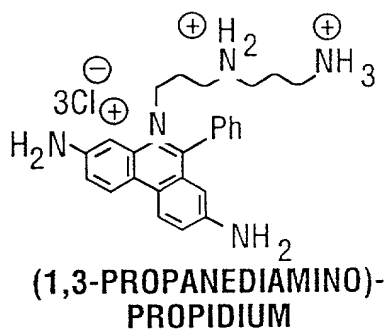
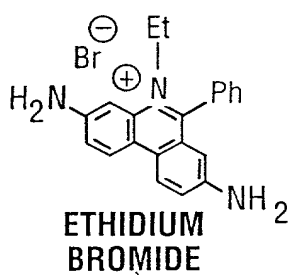


FIG. 66

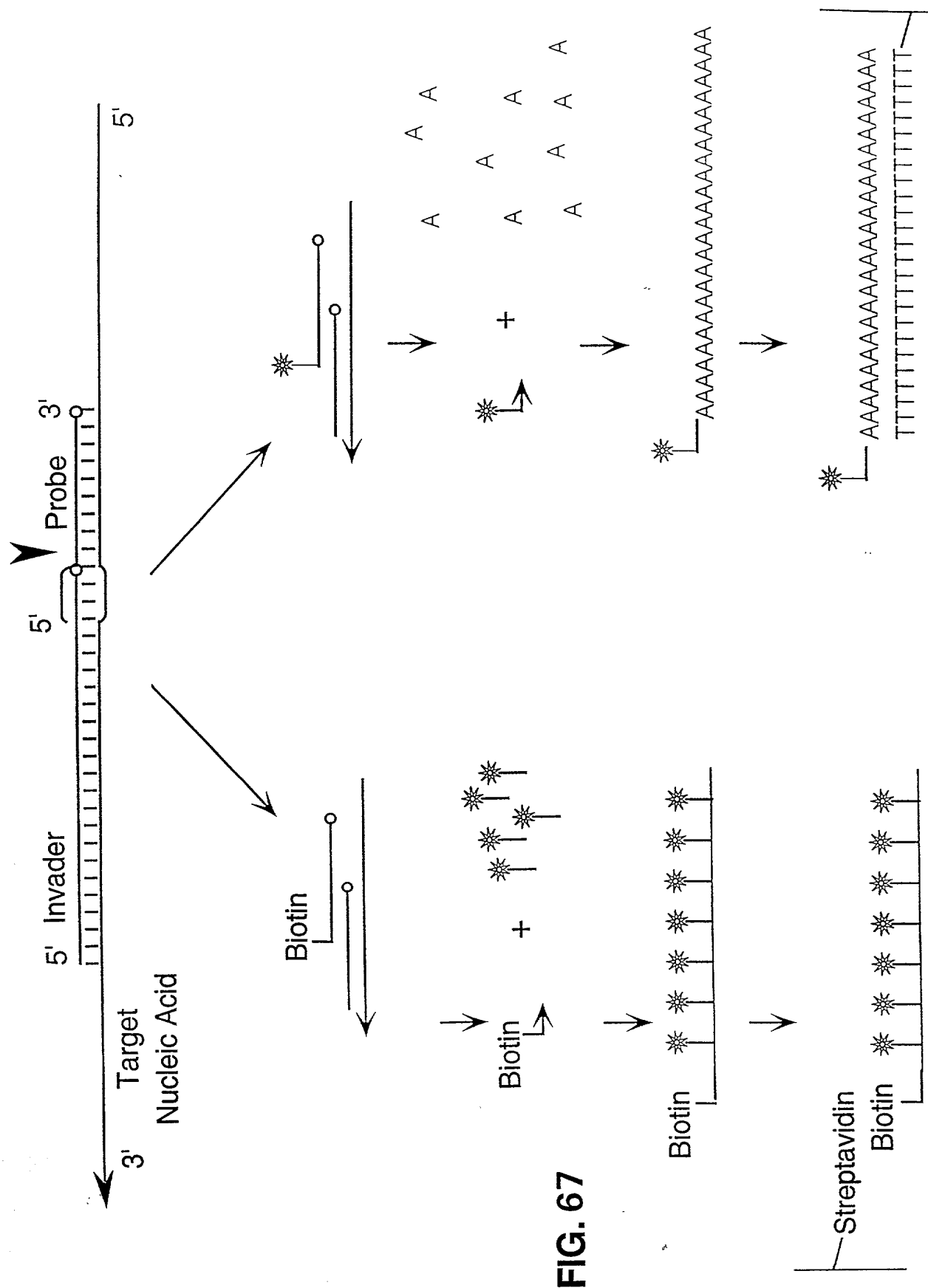


FIG. 67

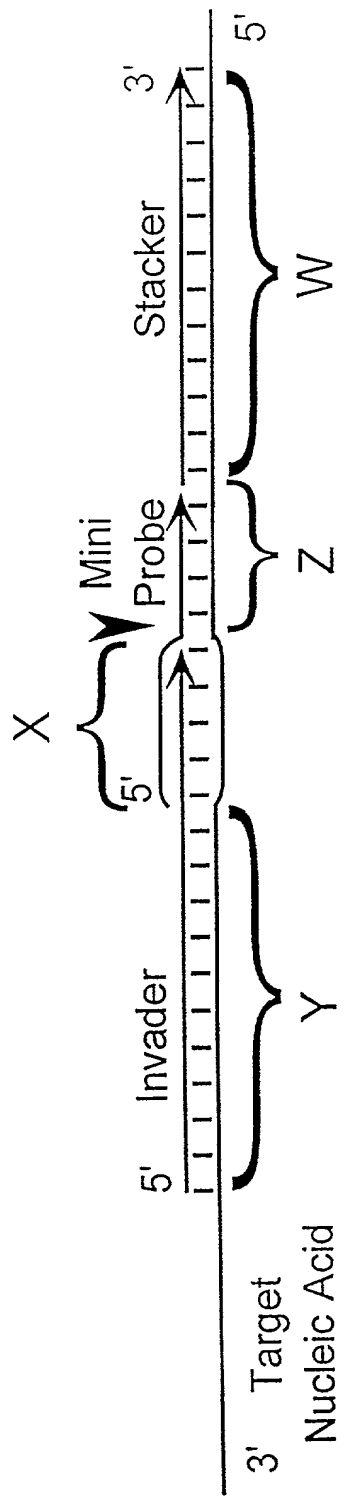
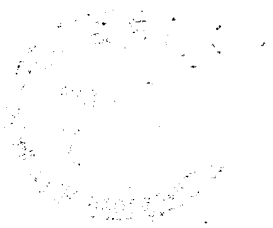


FIG. 68

10081805, 050702



FIG. 69



| | 10 | 20 | 30 | 40 | 50 | 60 | 70 | | |
|---|-------------|------------|----------|----------|----------|----------|-----------|---------------|-------------|
| 1 | MGVQ---- | FGDFIPK-- | NIISFEDL | KGKKVAID | GMNALYQF | LTSIRLDG | SPLNRKGE | ITSAYNGVFY | MJAFEN1.PRO |
| 1 | MGVP----- | IGEIIIPR-- | KEIELENL | YGKKIAID | ALNAIYQF | LSTIRQKD | GTPLMDSK | GRITSHLSGLFY | PFUFEN1.PRO |
| 1 | MGIQGLAKLI | ADVAPSAI | RENDIKSY | FGRKVAID | ASMSIYQF | LIAVRQ-- | GGDVLQNEE | GETTSHLMGMFY | HUMFEN1.PRO |
| 1 | MGIHGLAKLI | ADVAPSAI | RENDIKSY | FGRKVAID | ASMSIYQF | LIAVRQ-- | GGDVLQNEE | GETTSHLMGMFY | MUSFEN1.PRO |
| 1 | MGIKGLNAII | SEHVPSAI | RKSDIKSF | FGRKVAID | ASMSLYQF | LIAVRQDQ | GGQLTNEA | GETTSHLMGMFY | YST510.PRO |
| 1 | MGVHSFWDIAG | ----- | PTARPVR | LESLEDK | RMAVDASI | WIYQFLK | AVRDQEG | NAVKN----- | SHITGFFR |
| 1 | MGVSGLWNI | LE----- | PVKRPVK | LETLV | NKRLAID | ASIWIYQF | LKAVRD | KEGNQLKS----- | SHVVGFFR |
| 1 | MGVQGLWKLE | ----- | CSGROVS | PEALEG | KILAVD | ISILNQAL | KGVRDR | HGNSIEN----- | PHLLTLFH |
| 1 | MGVQGLWKLE | ----- | CSGHRVS | PEALEG | KVLAVD | ISILNQAL | KGVRDS | HGNVIEN----- | AHLLTLFH |
| 1 | MGVQGLWKLE | ----- | CSGRP | INPGT | LEGKIL | AVDISI | WLNAVK | GARDRQGN | AIQN----- |
| 1 | MTINGI | EWANHVV | ----- | RKVP | NETMRD | KTLSID | GHIWL | YESLKGCEA | HHQQT----- |
| | | | | | | | | | PNSYLVTFFT |
| | | | | | | | | | CELRAD2.PRO |

| | 80 | 90 | 100 | 110 | 120 | 130 | 140 |
|--|----|----|-----|-----|-----|-----|-----|
|--|----|----|-----|-----|-----|-----|-----|

| | | | | | | | | | | |
|----|------------|----------|---------|---------|---------|-------------|----------|------------|------------|-------------|
| 64 | KTIHLENDIT | PIWVFDGE | PPKLKEK | TRKVRRE | MEKEAEL | KMKEAIKK | ----- | EDFEEAAK | YAKRVSYLTP | MJAFEN1.PRO |
| 64 | RTINLMEAG | IKPVYVFD | GEPPF | KKKELEK | REAREE | AEEKWREALEK | ----- | GEIEEARK | YAQRATRVNE | PFUFEN1.PRO |
| 70 | RTIRMMENG | IKPVYVFD | GKPPQL | KSGELAK | RSERAE | AEKQLQQAQA | ----- | GAEQVEK | FTKRLVKVTK | HUMFEN1.PRO |
| 69 | RTIRM-ENG | IKPVYVFD | GKPPQL | KSGELAK | RSERAE | AEKQLQQAQA | ----- | GMEEEVEK | FTKRLVKVTK | MUSFEN1.PRO |
| 71 | RJLRMIDNG | IKPCYVFD | GKPPDL | KSHEL | TKRSSR | RVETEKLA | ----- | EA----- | TTELEKMK | QERRLVKVS |
| 61 | RICKLLYFG | IRPVFVFD | GVPVL | KRETI | RQKERR | QKRESAK | STARKLL | ALQLQNG | SNDNKRDS | DEVTM |
| 61 | RICKLLFFG | IKPVFVFD | GAPSL | KRQTI | QKQARR | LDREENAT | VTANKLL | ALQMRHQA | MLKRDAD | DEVTVQ |
| 61 | RLCKLLFFR | IRPIFVFD | GDAPLL | KKQTL | VKRRQR | KDLASSDS | RKTTTEK | LLKTF | LRQAIK | TERIAATVTG |
| 61 | RLCKLLFFR | IRPIFVFD | GDAPLL | KKQTL | AKRRQR | KDSASID | SRKTTTEK | LLKTF | LRQAL | KTDRIAASVTG |
| 61 | RLCKLLFFR | IRPIFVFD | GEAPLL | KKRQTL | AKRRQR | TDKASND | ARKTNEK | LLRTF | LRQAIK | AERIAATVTG |
| 60 | RIQRLLLEK | IIPIVVF | DNINASS | SAHESK | DQNEF | VPRKRR | SFGDSP | FTNLV----- | ----- | CELRAD2.PRO |

FIG. 70A

| | 150 | 160 | 170 | 180 | 190 | 200 | 210 |
|-----|--|-----|-----|-----|-----|-----|--------------|
| 130 | KMVENCKYLLSLMGIPYVEAPSEGEAQASYMAKKGDVAVVSQDYDALLYGAPRVVRNLTTTKEM----- | | | | | | MJAFEN1.PRO |
| 130 | MLIEDAKKLLLELMGIPVQAPSEGEAQAAAYMAAGSVYASASQDYDSLFGAPRLVRNLTIITGKRKLPGK | | | | | | PFUFEN1.PRO |
| 136 | QHNDECKHLLSLMGIPYLDAPSEAEASCAALVKAGKVAAATEDMDCLTFGSPVLMRHLTASEAKKLP IQ | | | | | | HUMFEN1.PRO |
| 134 | QHNDECKHLLSLMGIPYLDAPSEAEASCAALAKAGKVAAATEDMDCLTFGSPVLMRHLTASEAKKLP IQ | | | | | | MUSFEN1.PRO |
| 134 | EHNEEAQKLLGLMGIPYIIAPTEAEQAELAKKGKVAAASEMDTLCYRTPFLLRHLTFSEAKKEPIH | | | | | | YST510.PRO |
| 131 | DMIKEVQELLSRFGIPYITAPMEAEQAELQLNLVDGIITDDSDVFLFGGKIYKNMFHEKNY---VE | | | | | | YSTRAD2.PRO |
| 131 | VMIKECQELLRLFGLPYIVAPOEAEQAQCSKLELKLVDGIVTDDSDVFLFGGTRVYRNMFNQNKF---VE | | | | | | SPORAD13.PRO |
| 131 | QMFLESQELLRLFGIPYIQAPMEAEQAQCAILDLTDOQTSGITDDSDIWLFGARHVYRNFFNKNKF---VE | | | | | | HUMXPG.PRO |
| 131 | QMFLESQELLRLFGVPYIQAPMEAEAOCAVLDLSDQTSGITDDSDIWLFGARHVYKNFFNKNKF---VE | | | | | | MUSXPG.PRO |
| 131 | QMCLESQELLRLFGIPYIVAPMEAEQAQCAILDLTDOQTSGITDDSDIWLFGARHVYKNFFSQNKH---VE | | | | | | XENXPG.PRO |
| 111 | DHVYKTNALLTELGIKVIIPAGDGEAQCARLEQLGVTSGCITTDFFDYFLFGGKNLYRFDFTAGT----- | | | | | | CELRAD2.PRO |
| | 220 | 230 | 240 | 250 | 260 | 270 | 280 |
| 195 | -----PELIELNEVLEDLRISLDDLIDIAIFMGTDYNPGGV--K--GIGFKRAYELVRSGVAK--DV | | | | | | MJAFEN1.PRO |
| 200 | NVYVE-IKPELIILEEVLKELKTREKLIELAILVGTDYNPGGI--K--GIGLKKALEIVRHSKDPLAKF | | | | | | PFUFEN1.PRO |
| 206 | EFHLSRILQELGLNQEQFVDL CILLGSDYCESIRGIGPKRAVDLIQK--HKSIEEIVRRDPN-----KY | | | | | | HUMFEN1.PRO |
| 204 | EFHLSRVLQELGLNQEQFVDL CILLGSDYCESIRGIGAKRAVDLIQK--HKSIEEIVRRDPS-----KY | | | | | | MUSFEN1.PRO |
| 204 | EIDTELVLRLGLDLTIEQFVDL CIMGCDYCESIRGVGPVTALKLIK T--HGSIEKIVEFIESGESNNTKW | | | | | | YST510.PRO |
| 198 | FYDAESILKLLGLDRKNMIELAQLLGSDYTNGLKMGVPVSSIEVIAEF---GNLKNFKDWYNNGOFDK RK | | | | | | YSTRAD2.PRO |
| 198 | LYLMDDMKREFNVNQMDLIKLAHLGSDYTMGLSRVGPVLALEILHEFPDGTGLFEFKWQRLSTGHAS | | | | | | SPORAD13.PRO |
| 198 | YYQYVDFHNLGLDRNKLINLAYLLGSDYTEGIP TVGCVTAMEILNEFPFGHGLEPL LKFSEWHEAQKNP | | | | | | HUMXPG.PRO |
| 119 | YYQYVDFYSQLGLDRNKLINLAYLLGSDYTEGIP TVGCVTAMEILNEFPGRGLDPL LKFSEWHEAQNNK | | | | | | MUSXPG.PRO |
| 198 | YYQYADIHNOLGLDRSKLINLAYLLGSDYTEGIP TVGVVSAMEILNEFPGGGLEPL VKFKEWSEAQDK | | | | | | XENXPG.PRO |
| 175 | -----SSTACLDHIMHLSLRMF----- | | | | | | CELRAD2.PRO |

FIG. 70B

| | 290 | 300 | 310 | 320 | 330 | 340 | 350 |
|-----|---|------|-------------------------------|-----|-------------|-------------|--------------|
| 251 | LKKEVEYYDEIKRIFKEPKV----- | TD-- | NYSLSLKLDPKKEGIIKFLVDENDFN | YD | MJAFEN1.PRO | | |
| 265 | QKQSDVDLYAIKEFFLNPPV----- | TD-- | NYNLVWRDPDEEGILKFLCDEHDFSEE | | PFUFEN1.PRO | | |
| 269 | PVPENWLHKEAHQLFLEPEV----- | LD | PESVELKWSEPNEEEEIKFMCGEKQFSEE | | HUMFEN1.PRO | | |
| 267 | PVPENWLHKEAQQFLFLEPEV----- | VD | PESVELKWSEPNEEEEVKFMCGEKQFSEE | | MUSFEN1.PRO | | |
| 272 | KIPEDWPYKQARMLFLDPEV----- | ID | NEINLKWSPPEKELEIYLCDDKKFSEE | | YST510.PRO | | |
| 265 | QETENKFEKDLRKKLVNNEIILDDDFPSVMVYDAYMRPEVDHDTTPFVWGVDPDLMLRSFMKTQLGWPHE | | YSTRAD2.PRO | | | | |
| 268 | KNDVNTPVKKRINKLVGK-IILPSEFPNPLVDEAYLHPAVDDSKQSFQWGIPDLDELRLQFLMATVGSKQ | | SPORAD13.PRO | | | | |
| 268 | KIRPNPHDTKVKKKL--RTLQLTPGFPNPAVAEAYLKPVVDDSKGSFLWGKPDLDKIREFCQRYFGWNRT | | HUMXPG.PRO | | | | |
| 268 | KVAENPYDTKVKKKL--RKLQLTPGFPNPAVADAYLRPVVDDSRGSFLWGKPDVDKIREFCORYFGWNRM | | MUSXPG.PRO | | | | |
| 268 | KMRPNPNDTKVKKKL--RLLDLQSQFPNPAVASAYLKPVVDESASFWSGRPDLEQIREFCESRFGWYRL | | XENXPG.PRO | | | | |
| 194 | -----EKKVSRPHLIISTAILLGCDYFORGVQNIIGIVSVFD-ILGEFGDDGNEEIDPHVILDRFASVYRE | | CELRAD2.PRO | | | | |
| | 360 | 370 | 380 | 390 | 400 | 410 | 420 |
| 300 | RVKKHVDKLYNLIA----- | | | | | | MJAFEN1.PRO |
| 314 | RVKNGLERLKAI----- | | | | | | PFUFEN1.PRO |
| 320 | RIRSGVKRLSKSRQGS-TQGRLLDFFFKVT----- | | | | | | HUMFEN1.PRO |
| 318 | RIRSGVKRLSKSRQGS-TQGRLLDFFFKVT----- | | | | | | MUSFEN1.PRO |
| 323 | RVKSGISRLLKGLKSG-IQGRLLDGGFFOVV----- | | | | | | YST510.PRO |
| 335 | KSDEILIPLIRDVNKRKK----- | | | | | KGKQ | YSTRAD2.PRO |
| 337 | RTNEVLLPVIQDMHKKOF----- | | | | | VGTK | SPORAD13.PRO |
| 336 | KTDESLFPVLKQLDAQQTQLRIDSFFRLAQKEKEDAKRIKSQRLNRAVTCMLRKEKEAAASEIEAVSVAM | | | | | | HUMXPG.PRO |
| 336 | KTDESLYPVLKHLNAHQTLRIDSFFRLAQKEKQDAKLKSHRLSRAVTCMLRKEEKAPELTKVTEAM | | | | | | MUSXPG.PRO |
| 336 | KTDEVLLPVLKQLNAQQTLRIDSFFRLEQHEAAG---LKSQRLRAVTCMKRKERDVEAEVEAAVAVM | | | | | | XENXPG.PRO |
| 257 | EIPARSEDTRKRLRLRRKKYNFPVGFPCNDAVHNAITMYLRPPVSSEIPKIIPR----- | | | | | AANFQQVAEIM | CELRAD2.PRO |

FIG. 70C

| | 430 | 440 | 450 | 460 | 470 | 480 | 490 |
|-----|--|---|--------------|-------|-------|-----------|-------------|
| 314 | ----- | ----- | ----- | ----- | ----- | ----- | MJAFEN1.PRO |
| 327 | ----- | ----- | ----- | ----- | ----- | ----- | PFUFEN1.PRO |
| 348 | ----- | ----- | ----- | ----- | ----- | -----GSL | HUMFEN1.PRO |
| 346 | ----- | ----- | ----- | ----- | ----- | -----GSL | MUSFEN1.PRO |
| 351 | ----- | ----- | ----- | ----- | ----- | -----PK-T | YST510.PRO |
| 357 | KRINEFF | ----- | ----- | ----- | ----- | ----- | YSTRAD2.PRO |
| 359 | SNLTQFFEGGNTN | VYAPRVAYHFKSKRLENALSSFKNQISNQSPMSEIIQADADAFGESKGSDELOSRIL | SPORAD13.PRO | | | | |
| 406 | EKEFELLDKAKRK | TQKRGITNTLEESSLKRRLSDSKRNTCGGFLGETCLSESSDGSSEHAESSLM | HUMXPG.PRO | | | | |
| 406 | EKEFELDDAKGKTOKREL | PKYK-----KETSVPKRRRPSGNGGFLGDPYCESPQESSCEDGEGSSVM | MUSXPG.PRO | | | | |
| 403 | ERECTNQKKGQKNTKS | -----QGTKRRKPTCESQEDQDPGGGFIGIELKTLSSKAYSSD | XENXPG.PRO | | | | |
| 322 | MKECGWPATRTQKELALSIRRKVHLTTTVAQTRIPDFFAATKSKNFTPIVEPCE | SLIEDYISANN-----T | CELRAD2.PRO | | | | |

| | 500 | 510 | 520 | 530 | 540 | 550 | 560 |
|-----|---|-------------------------------|-------------------------------------|------------|-------|-------|------------------------------|
| 314 | ----- | ----- | ----- | ----- | ----- | ----- | NKTKQKTL MJAFEN1.PRO |
| 327 | ----- | ----- | ----- | ----- | ----- | ----- | KSGKQSTL PFUFEN1.PRO |
| 352 | SAKRKEPEPKGST | ----- | ----- | ----- | ----- | ----- | KKKAKTGAAG HUMFEN1.PRO |
| 350 | SAKRKEPEPKGPA | ----- | ----- | ----- | ----- | ----- | KKKAKTGGAG MUSFEN1.PRO |
| 354 | KEQLAAAKRAQE | ----- | ----- | ----- | ----- | ----- | NKKLNKNKNK YST510.PRO |
| 364 | ----- | ----- | PREYISGDKKLNTSKRISTATGKL | ----- | ----- | ----- | KK YSTRAD2.PRO |
| 429 | RRKKMMASKNSSDSDSEDN | FLASLTPKTNSSSISIENLPRKTKLSTSL | ----- | ----- | ----- | ----- | KKP SPORAD13.PRO |
| 476 | NVQRRTAAKEPKTSASDSONSVKEAPVKNGGATTSSSDSDDDGGKEKMLVLTARS | VFGKKRRKLRARG | HUMXPG.PRO | | | | |
| 469 | SARQRSAAESSKIGCDV | PDVLRDSPHGRQGC | VSTSSDSEDGEDKAKTVLVTARPVFGKKRRKLSMK | MUSXPG.PRO | | | |
| 458 | -----GSSSDAEDLPSGLIDKQSQSGIVGROKASNKVESSSDDEDR | TMVTAKPVFQKKTKSKTMKE | XENXPG.PRO | | | | |
| 387 | WMRKRKRSESPQILQHHAKRQVPDRK | ----- | ----- | ----- | ----- | ----- | RSVKIRAFKPYPTDVI CELRAD2.PRO |

FIG. 70D

202050" 908T800T

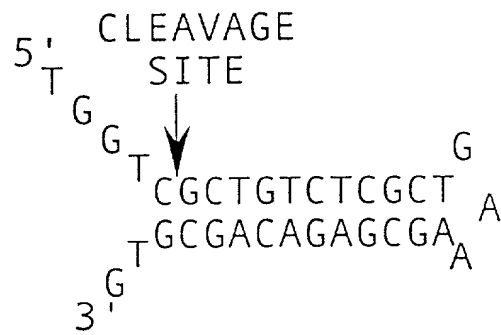
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335 ESWFKR
375 KFKRGK
373 KFRRGK
377 VTKGRR
390 ---RKM
483 SKRRRK
546 RKRKTZ
538 RRKKKT
523 TVKRK
429 ELGDSD

MJAFEN1.PRO
PFUFEN1.PRO
HUMFEN1.PRO
MUSFEN1.PRO
YST510.PRO
YSTRAD2.PRO
SPORAD13.PRO
HUMXPG.PRO
MUSXPG.PRO
XENXPG.PRO
CELRAD2.PRO

FIG. 70E

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S-33



11-8-0

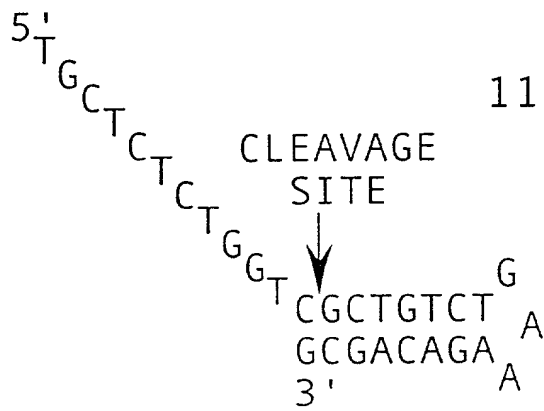


FIG. 71